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71)	Applicant (for all designated States except US):	ORIGENE TECHNOLOGIES, INC (USUS);	6 Taft Court, Suite 100, Rockville, MD 20850 (US).

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(75) Inventors/Applicants (or US only): SUN, Zailen [CN/US]; 1083 Copperstone Court, Rockville, MD 20852 (US). JAY, Gilbert [US/US]; 5801 Nicholson Lane, North Bethesda, MD 20852 (US).

(74) Agent: **LEBOVITZ, Richard, M.**; Origenc Technologies, Inc., 6 Taff Court, Suite 100, Rockville, MD 20850 (US).

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(57) Abstract: The present invention relates to all facets of novel polynucleotides, the polypeptides they encode, antibodies and specific binding partners thereto, and their applications to research, diagnosis, drug discovery, therapy, clinical medicine, forensic science and medicine, etc. The polynucleotides are differentially-regulated in prostate cancer and are therefore useful in variety of ways, including, but not limited to, as molecular markers, as drug targets, and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, determining predisposition to, etc., diseases and conditions, to prostate cancer.

## PROSTATE CANCER EXPRESSION PROFILES

This application claims the benefit U.S. Provisional Application No. 60/281,731, filed April 6, 2001, and U.S. Provisional Application No. 60/281,732, filed April 6, 2001, which are hereby incorporated by reference in their entirety.

### DESCRIPTION OF THE DRAWINGS

Tables 1 and 2 list genes differentially-regulated in prostate cancer. "DNA SEQ ID" and "Prt SEQ ID" refer to the corresponding DNA and protein sequences in the attached sequence listing. The genes can alternatively be referred to by GenBank accession number in the fifth column ("GI#") or the "Identifier" in the third column. The genes listed in Table 1 are up-regulated, and those in Table 2 are down-regulated ("Exp" refers to the expression profile, U is up-regulated expression, and D is down-regulated expression). The

GenBank. 5', 3', genomic sequences, etc., which correspond to the genes can be retrieved routinely from Genbank, e.g., by searching the accession number. SEQ ID NOS 1-107 are DNA, and 108-211 are polypeptide. These sequences, and all information referenced to the accession number, are incorporated by reference in their entirety.

The polypeptide sequences was analyzed for the presence of functional domains using the publicly available Pfam program. This information is summarized in Table 3. Domains present in each polypeptide are listed under "domain." Any abbreviations are those used in Pfam. The start of the domain is indicated by "seq-f" and the end of the domain by "seq-t." The "score" is the statistical score of this match to the domain in bits. In general, a higher score indicates a better match. "E" is the statistical score of this match in Evalue

(frequentist) approach. The smaller score in this case shows a better match between the domain and the query sequence. For more information on the program and scoring, see, e.g., Sonhammer et al., *Proteins: Structure, Function and Genetics* 28:405-420 (1997);

Sonhammer et al., *Nucleic Acids Research*, 26:320-322 (1998); Bateman et al., *Nucleic Acids Research*, 27:260-262 (1999); Bateman et al., *Nucleic Acids Research*, 28:263-266 (2000).

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## DESCRIPTION OF THE INVENTION

The present invention relates to all facets of novel polynucleotides, the polypeptides they encode, antibodies and specific binding partners thereto, and their applications to research, diagnosis, drug discovery, therapy, clinical medicine, forensic science and medicine, etc. The polynucleotides are differentially regulated in prostate cancer and are therefore useful in variety of ways, including, but not limited to, as molecular markers, as drug targets, and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, determining predisposition to, etc., diseases and conditions,, especially relating to prostate cancer. The identification of specific genes, and groups of genes, expressed in pathways physiologically relevant to prostate cancer permits the definition of functional and disease pathways, and the delineation of targets in these pathways which are useful in diagnostic, therapeutic, and clinical applications. The present invention also relates to methods of using the polynucleotides and related products (proteins, antibodies, etc.) in business and computer-related methods, e.g., advertising, displaying, offering, selling, etc., such products for sale, commercial use, licensing, etc.

Prostate cancer is the most common form of cancer diagnosed in the American male, occurring predominantly in males over age 50. The number of men diagnosed with prostate cancer has steadily increased as a result of the increasing population of older men. The American Cancer Society estimates that in the year 2000, about 180,000 American men were diagnosed with prostate cancer and about 32,000 died from the disease. In comparison, 1998 estimates for lung cancer in men were 171,500 cases and 160,100 deaths, and for colorectal cancer, the estimates were 131,600 cases and 56,000 deaths. Despite these high numbers, 89 percent of men diagnosed with the disease will survive at least five years and 63 percent will survive at least 10 years.

Patients having prostate cancer display a wide range of phenotypes. In some men, following detection, the tumor remains a latent histological tumor and does not become clinically significant. However, in other men, the tumor progresses rapidly, metastasizing and killing the patient in a relatively short time. Prostate cancer can be cured if the tumor is confined to a small region of the gland and is discovered at early stage. In such cases, radiation or surgical removal often results in complete elimination of the disease. Frequently, however, the prostate cancer has already spread to surrounding tissue and metastasized to

remote locations. In these cases, radiation and other therapies, are less likely to effect a complete cure.

Androgen deprivation is a conventional therapy to treat prostate cancer. Androgen blockade can be achieved through several different routes. Androgen suppressive drugs include, e.g., Lupron (leuprolide acetate), Casodex (bicalutamide), Eulexin (flutamide), Nilandron (nilutamide), Zoladex (goserelin acetate implant), and Viadur (leuprolide acetate), which act through several different mechanisms. While these drugs may offer remission and tumor regression in many cases, often the therapeutic effects are only temporary. Prostate tumors lose their sensitivity to such treatments, and become androgen-independent. Thus, new therapies are clearly needed.

The first clinical symptoms of prostate cancer are typically urinary disturbances, including painful and more frequent urination. Diagnosis for prostate cancer is usually accomplished using a combination of different procedures. Since the prostate is located next to the rectum, rectal digital examination allows the prostate to be examined manually for the presence of hyperplasia and abnormal tissue masses. Usually, this is the first line of detection. If a palpable mass is observed, a blood specimen can be assayed for prostate-specific antigen (PSA). Very little PSA is present in the blood of a healthy individual, but BPH and prostate cancer can cause large amounts of PSA to be released into the blood, indicating the presence of diseased tissue. Definitive diagnosis is generally accomplished by biopsy of the prostate tissue.

No single gene or protein has been identified which is responsible for the etiology of all prostate cancers. Although PSA is widely used as a diagnostic reagent, it has limitations in its sensitivity and its ability to detect early cancers. It is estimated that approximately 20% to 30% of tumors will be missed when PSA is used alone. It is likely that diagnostic and prognostic markers for prostate cancer disease will involve the identification and use of many different genes and gene products to reflect its multifactorial origin.

A continuing goal is to characterize the gene expression patterns of the various prostate cancers to genetically differentiate them, providing important guidance in preventing and treating cancers. Molecular pictures of cancer, such as the pattern of differentially-regulated genes identified herein, provide an important tool for molecularly dissecting and classifying cancer, identifying drug targets, providing prognosis and therapeutic information, etc. For instance, an array of polynucleotides corresponding to genes differentially regulated in prostate cancer can be used to screen tissue samples for the existence of cancer, to

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categorize the cancer (e.g., by the particular pattern observed), to grade the cancer (e.g., by the number of differentially-regulated genes and their amounts of expression), to identify the source of a secondary tumor, to screen for metastatic cells, etc. These arrays can be used in combination with other markers, e.g., PSA, PMSA (prostate membrane specific antigen), or any of the grading systems used in clinical medicine.

As indicated by these studies, cancer is a highly diverse disease. Although all cancers share certain characteristics, the underlying cause and disease progression can differ significantly from patient to patient. So far, over a dozen distinct genes have been identified which, when mutant, result in a cancer. In breast cancer, alone, a handful of different genes have been isolated which either cause the cancer, or produce a predisposition to it. As a consequence, disease phenotypes for a particular cancer do not look all the same. In addition to the differences in the gene(s) responsible for the cancer, heterogeneity among individuals, e.g., in age, health, sex, and genetic background, can also influence the disease and its progression. Gene penetrance, in particular, can vary widely among population members.

Recent studies have shown tremendous diversity in gene expression patterns among cancer patients. For these and other reasons, one gene/polypeptide target alone can be insufficient to diagnose or treat a cancer. Even a gene which is highly differentially-expressed and penetrant in cancer patients may not be so highly expressed in all patients and at all stages of the cancer. By selecting a set of genes and/or the polypeptides they encode, cancer diagnostics and therapeutics can be designed which effectively diagnose and treat a population of diseased individuals, rather than only a small handful when single genes are targeted.

#### Nucleic acids

In accordance with the present invention, genes have been identified which are differentially expressed in prostate cancer. Tables 1 and 2 list of genes which are differentially-regulated in the cancer. These genes can be further divided into groups based on additional characteristics of their expression and the tissues in which they are expressed. For instance, genes can be further subdivided based on the stage and/or grade of the cancer in which they are expressed. Genes can also be grouped based on their penetrance in a prostate cancer, e.g., expressed in all prostate cancer examined, expressed in a certain percentage of prostate cancer examined, etc. Additionally, genes can be categorized by their function and/or the polypeptides they encode. This includes, but is not limited to, cellular

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localization, functional activity (e.g., kinase, cytoskeletal element, or transcriptional factor), functional pathway (e.g., protein manufacture, cell signaling, cell movement, cell adhesion, responsiveness to cAMP, energy production, etc.), etc. These groupings do not restrict or limit the use such genes in therapeutic, diagnostic, prognostic, etc., applications. For instance, a gene which is expressed in only some cancers (e.g., incompletely penetrant) may be useful in therapeutic applications to treat a subset of cancers. Similarly, a co-penetrant gene, or a gene which is expressed in prostate cancer and other normal tissues, may be useful as a therapeutic or diagnostic, even if its expression pattern is not highly prostate specific. Thus, the uses of the genes or their products are not limited by their patterns of expression.

For genes which are differentially-regulated, gene and protein replacement therapies can be used therapeutically to restore expression levels to normal. When a protein product is to be administered, secreted proteins are more likely to be targets for replacement therapy than intracellular and membrane-bound proteins. For the latter classes, gene therapy may be a more effective means of delivery, e.g., administering a gene which is expressed inside a cell on or on its surface.

By the phrase "differential expression," it is meant that the levels of expression of a gene, as measured by its transcription or translation product, are different depending upon the specific cell-type or tissue (e.g., in an averaging assay that looks at a population of cells). There are no absolute amounts by which the gene expression levels must vary, as long as the differences are measurable.

The phrase "down-regulated" indicates that an mRNA transcript or other nucleic acid corresponding to a polynucleotide of the present invention is expressed in lower amounts in a cancer as compared to the same transcript expressed in normal cells from which the cancer was derived. In general, down-regulation can be assessed by any suitable method, including any of the nucleic acid detection and hybridization methods mentioned below, as well as polypeptide-based methods. Down-regulation also includes going from substantially no expression in a normal tissue, from detectable expression in a normal tissue, from significant expression in a normal tissue, to higher levels in the cancer.

The phrase "up-regulated" indicates that an mRNA transcript or other nucleic acid corresponding to a polynucleotide of the present invention is expressed in larger amounts in a cancer as compared to the same transcript expressed in normal cells from which the cancer was derived. For instance, a gene's up-regulation can be determined by comparing its abundance per gram of RNA (e.g., total RNA, polyadenylated mRNA, etc.) extracted from a

cancer tissue in comparison to the corresponding normal tissue. The normal tissue can be from the same or different individual or source. For convenience, it can be supplied as a separate component or in a kit in combination with probes and other reagents for detecting genes. The quantity by which a nucleic acid is up-regulated can be any value, e.g., more than 10%, 50%, 2-fold, 5-fold, 10-fold, etc. Up-regulation also includes going from substantially no expression, to detectable expression, to significant or highly restricted expression, etc.

Differential regulation can be determined by any suitable method, e.g., by comparing its abundance per gram of RNA (e.g., total RNA, polyadenylated mRNA, etc.) extracted from a prostate tissue in comparison to the corresponding normal tissue. The normal tissue can be from the same or different individual or source. For convenience, it can be supplied as a separate component or in a kit in combination with probes and other reagents for detecting genes. The quantity by which a nucleic acid is differentially-regulated can be any value, e.g., about 10% more or less of normal expression, about 50% more or less of normal expression, 2-fold more or less, 5-fold more or less, 10-fold more or less, etc.

The amount of transcript can also be compared to a different gene in the same sample, especially a gene whose abundance is known and substantially no different in its expression between normal and cancer cells (e.g., a "control" gene). If represented as a ratio, with the quantity of differentially-regulated gene transcript in the numerator and the control gene transcript in the denominator, the ratio would be larger, e.g., in breast cancer than in a sample from normal breast tissue.

Differential-regulation can arise through a number of different mechanisms. The present invention is not bound by any specific way through which it occurs. Differential-regulation of a polynucleotide can occur, e.g., by modulating (1) transcriptional rate of the gene (e.g., increasing its rate, inducing or stimulating its transcription from a basal, low-level rate, etc.), (2) the post-transcriptional processing of RNA transcripts, (3) the transport of RNA from the nucleus into the cytoplasm, (4) RNA nuclear and cytoplasmic turnover and polypeptide turnover (e.g., by virtue of having higher stability or resistance to degradation), and combinations thereof. See, e.g., Tollervey and Caceras, *Cell*, 103:703-709, 2000.

A differentially-regulated polynucleotide is useful in a variety of different applications as described in greater details below. Because it is more abundant in cancer, it and its expression products can be used in a diagnostic test to assay for the presence of cancer, e.g., in tissue sections, in a biopsy sample, in total RNA, in lymph, in blood, etc. Differentially-regulated polynucleotides and polypeptides can be used individually, or in

groups, to assess the cancer, e.g., to determine the specific type of cancer, its stage of development, the nature of the genetic defect, etc., or to assess the efficacy of a treatment modality. How to use polynucleotides in diagnostic and prognostic assays is discussed below. In addition, the polynucleotides and the polypeptides they encode, can serve as a target for therapy or drug discovery. A polypeptide, coded for by a differentially-regulated polynucleotide, which is displayed on the cell-surface, can be a target for immunotherapy to destroy, inhibit, etc., the diseased tissue. Differentially-regulated transcripts can also be used in drug discovery schemes to identify pharmacological agents which suppress, inhibit, etc., their differential-regulation, thereby preventing the phenotype associated with their expression. Thus, a differentially-regulated polynucleotide and its expression products of the present invention have significant applications in diagnostic, therapeutic, prognostic, drug development, and related areas.

The expression patterns of the differentially expressed genes disclosed herein can be described as a "fingerprint" in that they are a distinctive pattern displayed by a cancer. Just as with a fingerprint, an expression pattern can be used as a unique identifier to characterize the status of a tissue sample. The list of genes represented in Tables 1 and 2 provide an example of a cell expression profile for a prostate cancer. It can be used as a point of reference to compare and characterize unknown samples and samples for which further information is sought. Tissue fingerprints can be used in many ways, e.g., to classify an unknown tissue as being a prostate cancer, to determine the origin of a particular cancer (e.g., the origin of metastatic cells), to determine the presence of a cancer in a biopsy sample, to assess the efficacy of a cancer therapy in a human patient or a non-human animal model, to detect circulating cancer cells in blood or a lymph node biopsy, etc. While the expression profile of the complete gene set represented in Tables 1 and 2 may be most informative, a fingerprint containing expression information from less than the full collection can be useful, as well. In the same way that an incomplete fingerprint may contain enough of the pattern of whorls, arches, loops, and ridges, to identify the individual, a cell expression fingerprint containing less than the full complement may be adequate to provide useful and unique identifying and other information about the sample. Moreover, cancer is a multifactorial disease, involving genetic aberrations in more than gene locus. This multifaceted nature may be reflected in different cell expression profiles associated with breast cancers arising in different individuals, in different locations in the same individual, or even within the same cancer locus. As a result, a complete match with a particular cell expression profile, as



shown herein, is not necessary to classify a cancer as being of the same type or stage. Similarity to one cell expression profile, e.g., as compared to another, can be adequate to classify cancer types, grades, and stages. SEQ ID NOS 1-211 are referred to generally as "genes" to indicate that they represent specific gene loci, and are not limited to the particular nucleotide and polypeptide sequences disclosed herein. For example, fibronectin (SEQ ID NO 60 and 196) is up-regulated in prostate cancers. Probes to detect its up regulation can be selected from the attached specific sequences, as well as genomic, upstream, downstream, and intron sequences which are not in the attached sequence listing.

A mammalian polynucleotide, or fragment thereof, of the present invention is a polynucleotide having a nucleotide sequence obtainable from a natural source. It therefore includes naturally-occurring normal, naturally-occurring mutant, and naturally-occurring polymorphic alleles (e.g., SNPs), differentially-spliced transcripts, splice-variants, etc. By the term "naturally-occurring," it is meant that the polynucleotide is obtainable from a natural source, e.g., animal tissue and cells, body fluids, tissue culture cells, forensic samples. Natural sources include, e.g., living cells obtained from tissues and whole organisms, tumors, cultured cell lines, including primary and immortalized cell lines. Naturally-occurring mutations can include deletions (e.g., a truncated amino- or carboxy-terminus), substitutions, inversions, or additions of nucleotide sequence. These genes can be detected and isolated by polynucleotide hybridization according to methods which one skilled in the art would know, e.g., as discussed below.

A polynucleotide according to the present invention can be obtained from a variety of different sources. It can be obtained from DNA or RNA, such as polyadenylated mRNA or total RNA, e.g., isolated from tissues, cells, or whole organism. The polynucleotide can be obtained directly from DNA or RNA, from a cDNA library, from a genomic library, etc. The polynucleotide can be obtained from a cell or tissue (e.g., from an embryonic or adult tissues) at a particular stage of development, having a desired genotype, phenotype, disease status, etc.

The genes described in Tables 1 and 2 can be partial sequences that correspond to full-length, naturally-occurring transcripts. The present invention includes, as well, full-length polynucleotides that comprise these partial sequences, e.g., genomic DNAs and polynucleotides comprising a start and stop codon, a start codon and a polyA tail, a transcription start and a polyA tail, etc. These sequences can be obtained by any suitable method, e.g., using a partial sequence as a probe to select a full-length cDNA from a library

containing full-length inserts. A polynucleotide which "codes without interruption" refers to a polynucleotide having a continuous open reading frame ("ORF") as compared to an ORF which is interrupted by introns or other noncoding sequences.

## 5 Genomic

The present invention also relates genomic DNA from which the polynucleotides of the present invention can be derived. A genomic DNA coding for a human, mouse, or other mammalian polynucleotide, can be obtained routinely, for example, by screening a genomic library (e.g., a YAC library) with a polynucleotide of the present invention, or by searching nucleotide databases, such as GenBank and EMBL, for matches. Promoter and other regulatory regions can be identified upstream of coding and expressed RNAs, and assayed routinely for activity, e.g., by joining to a reporter gene (e.g., CAT, GPP, alkaline phosphatase, luciferase, galactosidase). A promoter obtained from a prostate selective gene can be used, e.g., in gene therapy to obtain tissue-specific expression of a heterologous gene (e.g., coding for a therapeutic product or cytotoxin).

## 15 Constructs

A polynucleotide of the present invention can comprise additional polynucleotide sequences, e.g., sequences to enhance expression, detection, uptake, cataloging, tagging, etc. A polynucleotide can include only coding sequence; a coding sequence and additional non-naturally occurring or heterologous coding sequence (e.g., sequences coding for leader, signal, secretory, targeting, enzymatic, fluorescent, antibiotic resistance, and other functional or diagnostic peptides); coding sequences and non-coding sequences, e.g., untranslated sequences at either a 5' or 3' end, or dispersed in the coding sequence, e.g., introns.

A polynucleotide according to the present invention also can comprise an expression control sequence operably linked to a polynucleotide as described above. The phrase "expression control sequence" means a polynucleotide sequence that regulates expression of a polypeptide coded for by a polynucleotide to which it is functionally ("operably") linked. Expression can be regulated at the level of the mRNA or polypeptide. Thus, the expression

control sequence includes mRNA-related elements and protein-related elements. Such elements include promoters, enhancers (viral or cellular), ribosome binding sequences, transcriptional terminators, etc. An expression control sequence is operably linked to a nucleotide coding sequence when the expression control sequence is positioned in such a

manner to effect or achieve expression of the coding sequence. For example, when a promoter is operably linked 5' to a coding sequence, expression of the coding sequence is driven by the promoter. Expression control sequences can include an initiation codon and additional nucleotides to place a partial nucleotide sequence of the present invention in-frame in order to produce a polypeptide (e.g., pET vectors from Promega have been designed to permit a molecule to be inserted into all three reading frames to identify the one that results in polypeptide expression). Expression control sequences can be heterologous or endogenous to the normal gene.

A polynucleotide of the present invention can also comprise nucleic acid vector sequences, e.g., for cloning, expression, amplification, selection, etc. Any effective vector can be used. A vector is, e.g., a polynucleotide molecule which can replicate autonomously in a host cell, e.g., containing an origin of replication. Vectors can be useful to perform manipulations, to propagate, and/or obtain large quantities of the recombinant molecule in a desired host. A skilled worker can select a vector depending on the purpose desired, e.g., to propagate the recombinant molecule in bacteria, yeast, insect, or mammalian cells. The following vectors are provided by way of example. Bacterial: pQE70, pQE60, pQE-9 (Qiagen), pBS, pD10, Phagescript, phiX174, pBK Phagemid, pNH8A, pNH16a, pNH18Z, pNH46A (Stratagene); Bluescript KS-II (Stratagene); pirc99a, pKK223-3, pKK233-3, pDR54 0, pRITS (Pharmacia). Eukaryotic: PWLNEO, pSV2CAT, pOG44, pXT1, pSG (Stratagene), pSVK3, PBPV, PMSG, pSVL (Pharmacia), pCR2.1/TOPO, pCRII/TOPO, pCR4/TOPO, pTrcHisB, pCMV6-XL4, etc. However, any other vector, e.g., plasmids, viruses, or parts thereof, may be used as long as they are replicable and viable in the desired host. The vector can also comprise sequences which enable it to replicate in the host whose genome is to be modified.

## Hybridization

Polynucleotide hybridization, as discussed in more detail below, is useful in a variety of applications, including, in gene detection methods, for identifying mutations, for making mutations, to identify homologs in the same and different species, to identify related members of the same gene family, in diagnostic and prognostic assays, in therapeutic applications (e.g., where an antisense polynucleotide is used to inhibit expression), etc.

The ability of two single-stranded polynucleotide preparations to hybridize together is a measure of their nucleotide sequence complementarity, e.g., base-pairing between nucleotides, such as A-T, G-C, etc. The invention thus also relates to polynucleotides, and their complements, which hybridize to a polynucleotide comprising a nucleotide sequence as set forth in Tables 1 and 2 and genomic sequences thereof. A nucleotide sequence hybridizing to the latter sequence will have a complementary polynucleotide strand, or act as a template for one in the presence of a polymerase (i.e., an appropriate polynucleotide synthesizing enzyme). The present invention includes both strands of polynucleotide, e.g., a sense strand and an anti-sense strand.

Hybridization conditions can be chosen to select polynucleotides which have a desired amount of nucleotide complementarity with the nucleotide sequences set forth in Tables 1 and 2 and genomic sequences thereof. A polynucleotide capable of hybridizing to such sequence, preferably, possesses, e.g., about 70%, 75%, 80%, 85%, 87%, 90%, 92%, 95%, 97%, 99%, or 100% complementarity, between the sequences. The present invention particularly relates to polynucleotide sequences which hybridize to the nucleotide sequences set forth in Tables 1 and 2 or genomic sequences thereof, under low or high stringency conditions. These conditions can be used, e.g., to select corresponding homologs in non-human species.

Polynucleotides which hybridize to polynucleotides of the present invention can be selected in various ways. Filter-type blots (i.e., matrices containing polynucleotide, such as nitrocellulose), glass chips, and other matrices and substrates comprising polynucleotides (short or long) of interest, can be incubated in a prehybridization solution (e.g., 6X SSC, 0.5% SDS, 100 µg/ml denatured salmon sperm DNA, 5X Denhardt's solution, and 50% formamide), at 22-68°C, overnight, and then hybridized with a detectable polynucleotide probe under conditions appropriate to achieve the desired stringency. In general, when high homology or sequence identity is desired, a high temperature can be used (e.g., 65 °C). As the homology drops, lower washing temperatures are used. For salt concentrations, the lower the salt concentration, the higher the stringency. The length of the probe is another consideration. Very short probes (e.g., less than 100 base pairs) are washed at lower temperatures, even if the homology is high. With short probes, formamide can be omitted. See, e.g., *Current Protocols in Molecular Biology*, Chapter 6, Screening of Recombinant Libraries; Sambrook et al., *Molecular Cloning*, 1989, Chapter 9.

For instance, high stringency conditions can be achieved by incubating the blot overnight (e.g., at least 12 hours) with a long polynucleotide probe in a hybridization solution containing, e.g., about 5X SSC, 0.5% SDS, 100 µg/ml denatured salmon sperm DNA and 50% formamide, at 42°C. Blots can be washed at high stringency conditions that allow, e.g., for less than 5% bp mismatch (e.g., wash twice in 0.1% SSC and 0.1% SDS for 30 min at 65°C), i.e., selecting sequences having 95% or greater sequence identity.

Other non-limiting examples of high stringency conditions includes a final wash at 65°C in aqueous buffer containing 30 mM NaCl and 0.5% SDS. Another example of high stringent conditions is hybridization in 7% SDS, 0.5 M NaPO<sub>4</sub>, pH 7, 1 mM EDTA at 50°C, e.g., overnight, followed by one or more washes with a 1% SDS solution at 42°C.

Whereas high stringency washes can allow for less than 5% mismatch, reduced or low stringency conditions can permit up to 20% nucleotide mismatch. Hybridization at low stringency can be accomplished as above, but using lower formamide conditions, lower temperatures and/or lower salt concentrations, as well as longer periods of incubation time.

Hybridization can also be based on a calculation of melting temperature (T<sub>m</sub>) of the hybrid formed between the probe and its target, as described in Sambrook et al..

Generally, the temperature T<sub>m</sub> at which a short oligonucleotide (containing 18 nucleotides or fewer) will melt from its target sequence is given by the following equation: T<sub>m</sub> = (number of A's and T's) × 2°C + (number of C's and G's) × 4°C. For longer molecules,  $T_m = 81.5 + 16.6 \log_{10} [Na^+] + 0.41(\%GC) - 600/N$  where [Na<sup>+</sup>] is the molar concentration of sodium ions, %GC is the percentage of GC base pairs in the probe, and N is the length. Hybridization can be carried out at several degrees below this temperature to ensure that the probe and target can hybridize. Mismatches can be allowed for by lowering the temperature even further.

Stringent conditions can be selected to isolate sequences, and their complements, which have, e.g., at least about 90%, 95%, or 97%, nucleotide complementarity between the probe (e.g., a short polynucleotide of Tables 1 and 2 or genomic sequences thereof) and a target polynucleotide.

Other homologs of polynucleotides of the present invention can be obtained from mammalian and non-mammalian sources according to various methods. For example, hybridization with a polynucleotide can be employed to select homologs, e.g., as described in Sambrook et al., *Molecular Cloning*, Chapter 11, 1989. Such homologs can have varying amounts of nucleotide and amino acid sequence identity and similarity to such

polynucleotides of the present invention. Mammalian organisms include, e.g., mice, rats, monkeys, pigs, cows, etc. Non-mammalian organisms include, e.g., vertebrates, invertebrates, zebra fish, chicken, *Drosophila*, *C. elegans*, *Xenopus*, yeast such as *S. pombe*, *S. cerevisiae*, roundworms, prokaryotes, plants, *Arabidopsis*, *artemia*, viruses, etc. The degree of nucleotide sequence identity between human and mouse can be about, e.g. 70% or more, 85% or more for open reading frames, etc.

# Alignment

Alignments can be accomplished by using any effective algorithm. For pairwise alignments of DNA sequences, the methods described by Wilbur-Lipman (e.g., Wilbur and Lipman, *Proc. Natl. Acad. Sci.*, 80:726-730, 1983) or Martinez/Needleman-Wunsch (e.g., Martinez, *Nucleic Acid Res.*, 11:4629-4634, 1983) can be used. For instance, if the Martinez/Needleman-Wunsch DNA alignment is applied, the minimum match can be set at 9, gap penalty at 1.10, and gap length penalty at 0.33. The results can be calculated as a similarity index, equal to the sum of the matching residues divided by the sum of all residues and gap characters, and then multiplied by 100 to express as a percent. Similarity index for related genes at the nucleotide level in accordance with the present invention can be greater than 70%, 80%, 85%, 90%, 95%, 99%, or more. Pairs of protein sequences can be aligned by the Lipman-Pearson method (e.g., Lipman and Pearson, *Science*, 227:1435-1441, 1985) with k-tuple set at 2, gap penalty set at 4, and gap length penalty set at 12. Results can be expressed as percent similarity index, where related genes at the amino acid level in accordance with the present invention can be greater than 65%, 70%, 75%, 80%, 85%, 90%, 95%, 99%, or more. Various commercial and free sources of alignment programs are available, e.g., MegAlign by DNA Star, BLAST (National Center for Biotechnology Information), BCM (Baylor College of Medicine) Launcher, etc.

Percent sequence identity can also be determined by other conventional methods, e.g., as described in Altschul et al., *Bull. Math. Bio.* 48: 603-616, 1986 and Henikoff and Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915-10919, 1992.

# Specific polynucleotide probes

A polynucleotide of the present invention can comprise any continuous nucleotide sequence of Tables 1 and 2, sequences which share sequence identity thereto, or complements thereof. The term "probe" refers to any substance that can be used to detect,

identify, isolate, etc., another substance. A polynucleotide probe is comprised of nucleic acid can be used to detect, identify, etc., other nucleic acids, such as DNA and RNA.

These polynucleotides can be of any desired size that is effective to achieve the specificity desired. For example, a probe can be from about 7 or 8 nucleotides to several thousand nucleotides, depending upon its use and purpose. For instance, a probe used as a primer PCR can be shorter than a probe used in an ordered array of polynucleotide probes. Probe sizes vary, and the invention is not limited in any way by their size. e.g., probes can be from about 7-2000 nucleotides, 7-1000, 8-700, 8-600, 8-500, 8-400, 8-300, 8-150, 8-100, 8-75, 7-50, 10-25, 14-16, at least about 8, at least about 10, at least about 15, at least about 25, etc. The polynucleotides can have non-naturally-occurring nucleotides, e.g., inosine, AZT, 3TC, etc. The polynucleotides can have 100% sequence identity or complementarity to a sequence of Tables 1 and 2, or it can have mismatches or nucleotide substitutions, e.g., 1, 2, 3, 4, or 5 substitutions. The probes can be single-stranded or double-stranded.

In accordance with the present invention, a polynucleotide can be present in a kit, where the kit includes, e.g., one or more polynucleotides, a desired buffer (e.g., phosphate, tris, etc.), detection compositions, RNA or cDNA from different tissues to be used as controls, libraries, etc. The polynucleotide can be labeled or unlabeled, with radioactive or non-radioactive labels as known in the art. Kits can comprise one or more pairs of polynucleotides for amplifying nucleic acids specific for differentially-regulated genes of the present invention, e.g., comprising a forward and reverse primer effective in PCR. These include both sense and anti-sense orientations. For instance, in PCR-based methods (such as RT-PCR), a pair of primers are typically used, one having a sense sequence and the other having an antisense sequence.

Another aspect of the present invention is a nucleotide sequence that is specific to, or for, a selective polynucleotide. The phrases "specific for" or "specific to" a polynucleotide have a functional meaning that the polynucleotide can be used to identify the presence of one or more target genes in a sample. It is specific in the sense that it can be used to detect polynucleotides above background noise ("non-specific binding"). A specific sequence is a defined order of nucleotides which occurs in the polynucleotide, e.g., in the nucleotide sequences of Tables 1 and 2. A probe or mixture of probes can comprise a sequence or sequences that are specific to a plurality of target sequences, e.g., where the sequence is a consensus sequence, a functional domain, etc., e.g., capable of recognizing a family of related genes. Such sequences can be used as probes in any of the methods described herein or

incorporated by reference. Both sense and antisense nucleotide sequences are included. A specific polynucleotide according to the present invention can be determined routinely.

A polynucleotide comprising a specific sequence can be used as a hybridization probe to identify the presence of, e.g., human or mouse polynucleotide, in a sample comprising a mixture of polynucleotides, e.g., on a Northern blot. Hybridization can be performed under high stringent conditions (see, above) to select polynucleotides (and their complements which can contain the coding sequence) having at least 90%, 95%, 99%, etc., identity (i.e., complementarity) to the probe, but less stringent conditions can also be used. A specific polynucleotide sequence can also be fused in-frame, at either its 5' or 3' end, to various nucleotide sequences as mentioned throughout the patent, including coding sequences for enzymes, detectable markers, GFP, etc, expression control sequences, etc.

A polynucleotide probe, especially one that is specific to a polynucleotide of the present invention, can be used in gene detection and hybridization methods as already described. In one embodiment, a specific polynucleotide probe can be used to detect whether a particular tissue or cell-type is present in a target sample. To carry out such a method, a selective polynucleotide can be chosen which is characteristic of the desired target tissue. Such polynucleotide is preferably chosen so that it is expressed or displayed in the target tissue, but not in other tissues which are present in the sample. For instance, if detection of prostate is desired, it may not matter whether the selective polynucleotide is expressed in other tissues, as long as it is not expressed in cells normally present in blood, e.g., peripheral blood mononuclear cells. Starting from the selective polynucleotide, a specific polynucleotide probe can be designed which hybridizes (if hybridization is the basis of the assay) under the hybridization conditions to the selective polynucleotide, whereby the presence of the selective polynucleotide can be determined.

Probes which are specific for polynucleotides of the present invention can also be prepared using involve transcription-based systems, e.g., incorporating an RNA polymerase promoter into a selective polynucleotide of the present invention, and then transcribing anti-sense RNA using the polynucleotide as a template. See, e.g., U.S. Pat. No. 5,545,522.

#### Polynucleotide composition

A polynucleotide according to the present invention can comprise, e.g., DNA, RNA, synthetic polynucleotide, peptide polynucleotide, modified nucleotides, dsDNA, ssDNA, ssRNA, dsRNA, and mixtures thereof. A polynucleotide can be single- or double-stranded,

triplex, DNA:RNA, duplexes, comprise hairpins, and other secondary structures, etc. Nucleotides comprising a polynucleotide can be joined via various known linkages, e.g., ester, sulfamate, sulfamide, phosphorothioate, phosphoramidate, methylphosphonate, carbamate, etc., depending on the desired purpose, e.g., resistance to nucleases, such as RNAse H, improved in vivo stability, etc. See, e.g., U.S. Pat. No. 5,378,825. Any desired nucleotide or nucleotide analog can be incorporated, e.g., 6-mercaptopguanine, 8-oxo-guanine, etc.

Various modifications can be made to the polynucleotides, such as attaching detectable markers (avidin, biotin, radioactive elements, fluorescent tags and dyes, energy transfer labels, energy-emitting labels, binding partners, etc.) or moieties which improve hybridization, detection, and/or stability. The polynucleotides can also be attached to solid supports, e.g., nitrocellulose, magnetic or paramagnetic microspheres (e.g., as described in U.S. Pat. No. 5,411,863; U.S. Pat. No. 5,543,289; for instance, comprising ferromagnetic, supermagnetic, paramagnetic, superparamagnetic, iron oxide and polysaccharide), nylon, agarose, diazotized cellulose, latex solid microspheres, polyacrylamides, etc., according to a desired method. See, e.g., U.S. Pat. Nos. 5,470,967, 5,476,925, and 5,478,893.

Polynucleotide according to the present invention can be labeled according to any desired method. The polynucleotide can be labeled using radioactive tracers such as  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^3\text{H}$ , or  $^{14}\text{C}$ , to mention some commonly used tracers. The radioactive labeling can be carried out according to any method, such as, for example, terminal labeling at the 3' or 5' end using a radiolabeled nucleotide, polynucleotide kinase (with or without dephosphorylation with a phosphatase) or a ligase (depending on the end to be labeled). A non-radioactive labeling can also be used, combining a polynucleotide of the present invention with residues having immunological properties (antigens, haptens), a specific affinity for certain reagents (ligands), properties enabling detectable enzyme reactions to be completed (enzymes or coenzymes, enzyme substrates, or other substances involved in an enzymatic reaction), or characteristic physical properties, such as fluorescence or the emission or absorption of light at a desired wavelength, etc.

### 30 Nucleic acid detection methods

Another aspect of the present invention relates to methods and processes for detecting differentially-regulated genes of the present invention. Detection methods have a variety of applications, including for diagnostic, prognostic, forensic, and research applications. To

accomplish gene detection, a polynucleotide in accordance with the present invention can be used as a "probe." The term "probe" or "polynucleotide probe" has its customary meaning in the art, e.g., a polynucleotide which is effective to identify (e.g., by hybridization), when used in an appropriate process, the presence of a target polynucleotide to which it is designed.

Identification can involve simply determining presence or absence, or it can be quantitative, e.g., in assessing amounts of a gene or gene transcript present in a sample. Probes can be useful in a variety of ways, such as for diagnostic purposes, to identify homologs, and to detect, quantitate, or isolate a polynucleotide of the present invention in a test sample.

Assays can be utilized which permit quantification and/or presence/absence detection of a target nucleic acid in a sample. Assays can be performed at the single-cell level, or in a sample comprising many cells, where the assay is "averaging" expression over the entire collection of cells and tissue present in the sample. Any suitable assay format can be used, including, but not limited to, e.g., Southern blot analysis, Northern blot analysis, polymerase chain reaction ("PCR") (e.g., Saiki et al., *Science*, 241:53, 1988; U.S. Pat. Nos. 4,683,195, 4,683,202, and 6,040,166; *PCR Protocols: A Guide to Methods and Applications*, Innis et al., eds., Academic Press, New York, 1990), reverse transcriptase polymerase chain reaction ("RT-PCR"), anchored PCR, rapid amplification of cDNA ends ("RACE") (e.g., Schaefer in *Gene Cloning and Analysis: Current Innovations*, Pages 99-115, 1997), ligase chain reaction ("LCR") (EP 320 308), one-sided PCR (Ohara et al., *Proc. Natl. Acad. Sci.*, 86:5673-5677, 1989), indexing methods (e.g., U.S. Pat. No. 5,508,169), *in situ* hybridization, differential display (e.g., Liang et al., *Nucl. Acid. Res.*, 21:3269-3275, 1993; U.S. Pat. Nos. 5,262,311, 5,599,672 and 5,965,409; WO97/18454; Prashar and Weissman, *Proc. Natl. Acad. Sci.*, 93:659-663, and U.S. Pat. Nos. 6,010,850 and 5,712,126; Welsh et al., *Nucleic Acid Res.*, 20:4965-4970, 1992, and U.S. Pat. No. 5,487,985) and other RNA fingerprinting techniques, nucleic acid sequence based amplification ("NASBA") and other transcription based amplification systems (e.g., U.S. Pat. Nos. 5,409,818 and 5,554,527; WO 88/10315), polynucleotide arrays (e.g., U.S. Pat. Nos. 5,143,854, 5,424,186; 5,700,637, 5,874,219, and 6,054,270; PCT WO 92/10092; PCT WO 90/15070), Qbeta Replicase (PCT/US87/00880), Strand Displacement Amplification ("SDA"), Repair Chain Reaction ("RCR"), nuclease protection assays, subtraction-based methods, Rapid-Scan™, etc. Additional useful methods include, but are not limited to, e.g., template-based amplification methods, competitive PCR (e.g., U.S. Pat. No. 5,747,251), redox-based assays (e.g., U.S. Pat. No. 5,871,918), Taqman-based assays (e.g., Holland et al., *Proc. Natl. Acad. Sci.*, 88:7276-7280, 1991; U.S. Pat. Nos.

5,210,015 and 5,994,063), real-time fluorescence-based monitoring (e.g., U.S. Pat. 5,928,907), molecular energy transfer labels (e.g., U.S. Pat. Nos. 5,348,853, 5,532,129, 5,565,322, 6,030,787, and 6,117,635; Tyagi and Kramer, *Nature Biotech.*, 14:303-309, 1996). Any method suitable for single cell analysis of gene or protein expression can be used, including in situ hybridization, immunocytochemistry, MACS, FACS, flow cytometry, etc. For single cell assays, expression products can be measured using antibodies, PCR, or other types of nucleic acid amplification (e.g., Brady et al., *Methods Mol. & Cell. Biol.* 2, 17-25, 1990; Eberwine et al., 1992, *Proc. Natl. Acad. Sci.*, 89, 3010-3014, 1992; U.S. Pat. No. 5,723,290). These and other methods can be carried out conventionally, e.g., as described in the mentioned publications.

Many of such methods may require that the polynucleotide is labeled, or comprises a particular nucleotide type useful for detection. The present invention includes such modified polynucleotides that are necessary to carry out such methods. Thus, polynucleotides can be DNA, RNA, DNA:RNA hybrids, PNA, etc., and can comprise any modification or substituent which is effective to achieve detection.

Detection can be desirable for a variety of different purposes, including research, diagnostic, prognostic, and forensic. For diagnostic purposes, it may be desirable to identify the presence or quantity of a polynucleotide sequence in a sample, where the sample is obtained from tissue, cells, body fluids, etc. In a preferred method as described in more detail below, the present invention relates to a method of detecting a polynucleotide comprising, contacting a target polynucleotide in a test sample with a polynucleotide probe under conditions effective to achieve hybridization between the target and probe; and detecting hybridization.

Any test sample in which it is desired to identify a polynucleotide or polypeptide thereof can be used, including, e.g., blood, urine, saliva, stool (for extracting nucleic acid, see, e.g., U.S. Pat. No. 6,177,251), swabs comprising tissue, biopsied tissue, tissue sections, cultured cells, etc.

Detection can be accomplished in combination with polynucleotide probes for other genes, e.g., genes which are expressed in other disease states, tissues, cells, such as brain, heart, kidney, spleen, thymus, liver, stomach, small intestine, colon, muscle, lung, testis, placenta, pituitary, thyroid, skin, adrenal gland, pancreas, salivary gland, uterus, ovary, prostate gland, peripheral blood cells (T-cells, lymphocytes, etc.), embryo, normal breast fat,

adult and embryonic stem cells, specific cell-types, such as endothelial, epithelial, myocytes, adipose, luminal epithelial, basoepithelial, myoepithelial, stromal cells, etc.

Polynucleotides can be used in wide range of methods and compositions, including for detecting, diagnosing, staging, grading, assessing, prognosticating, etc. diseases and disorders associated with differentially-regulated genes of the present invention, for monitoring or assessing therapeutic and/or preventative measures, in ordered arrays, etc. Any method of detecting genes and polynucleotides of Tables 1 and 2 can be used; certainly, the present invention is not to be limited how such methods are implemented.

Along these lines, the present invention relates to methods of detecting differentially-regulated genes described herein in a sample comprising nucleic acid. Such methods can comprise one or more the following steps in any effective order, e.g., contacting said sample with a polynucleotide probe under conditions effective for said probe to hybridize specifically to nucleic acid in said sample, and detecting the presence or absence of probe hybridized to nucleic acid in said sample, wherein said probe is a polynucleotide which is Tables 1 and 2, a polynucleotide having, e.g., about 70%, 80%, 85%, 90%, 95%, 99%, or more sequence identity thereto, effective or specific fragments thereof, or complements thereto. The detection method can be applied to any sample, e.g., cultured primary, secondary, or established cell lines, tissue biopsy, blood, urine, stool, and other bodily fluids, for any purpose.

Contacting the sample with probe can be carried out by any effective means in any effective environment. It can be accomplished in a solid, liquid, frozen, gaseous, amorphous, solidified, coagulated, colloid, etc., mixtures thereof, matrix. For instance, a probe in an aqueous medium can be contacted with a sample which is also in an aqueous medium, or which is affixed to a solid matrix, or vice-versa.

Generally, as used throughout the specification, the term "effective conditions" means, e.g., the particular milieu in which the desired effect is achieved. Such a milieu, includes, e.g., appropriate buffers, oxidizing agents, reducing agents, pH, co-factors, temperature, ion concentrations, suitable age and/or stage of cell (such as, in particular part of the cell cycle, or at a particular stage where particular genes are being expressed) where cells are being used, culture conditions (including substrate, oxygen, carbon dioxide, etc.). When hybridization is the chosen means of achieving detection, the probe and sample can be combined such that the resulting conditions are functional for said probe to hybridize specifically to nucleic acid in said sample.

The phrase "hybridize specifically" indicates that the hybridization between single-stranded polynucleotides is based on nucleotide sequence complementarity. The effective conditions are selected such that the probe hybridizes to a preselected and/or definite target nucleic acid in the sample. For instance, if detection of a gene set forth in Tables 1 and 2 is desired, a probe can be selected which can hybridize to such target gene under high stringent conditions, without significant hybridization to other genes in the sample. To detect homologs of a gene set forth in Tables 1 and 2, the effective hybridization conditions can be less stringent, and/or the probe can comprise codon degeneracy, such that a homolog is detected in the sample.

As already mentioned, the methods can be carried out by any effective process, e.g., by Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, *in situ* hybridization, etc., as indicated above. When PCR based techniques are used, two or more probes are generally used. One probe can be specific for a defined sequence which is characteristic of a selective polynucleotide, but the other probe can be specific for the selective polynucleotide, or specific for a more general sequence, e.g., a sequence such as polyA which is characteristic of mRNA, a sequence which is specific for a promoter, ribosome binding site, or other transcriptional features, a consensus sequence (e.g., representing a functional domain). For the former aspects, 5' and 3' probes (e.g., polyA, Kozak, etc.) are preferred which are capable of specifically hybridizing to the ends of transcripts. When PCR is utilized, the probes can also be referred to as "primers" in that they can prime a DNA polymerase reaction.

In addition to testing for the presence or absence of polynucleotides, the present invention also relates to determining the amounts at which polynucleotides of the present invention are expressed in sample and determining the differential expression of such polynucleotides in samples. Such methods can involve substantially the same steps as described above for presence/absence detection, e.g., contacting with probe, hybridizing, and detecting hybridized probe, but using more quantitative methods and/or comparisons to standards.

The amount of hybridization between the probe and target can be determined by any suitable methods, e.g., PCR, RT-PCR, RACE PCR, Northern blot, polynucleotide microarrays, Rapid-Scan, etc., and includes both quantitative and qualitative measurements. For further details, see the hybridization methods described above and below. Determining by such hybridization whether the target is differentially expressed (e.g., up-regulated or

differentially-regulated) in the sample can also be accomplished by any effective means. For instance, the target's expression pattern in the sample can be compared to its pattern in a known standard, such as in a normal tissue, or it can be compared to another gene in the same sample. When a second sample is utilized for the comparison, it can be a sample of normal tissue that is known not to contain diseased cells. The comparison can be performed on samples which contain the same amount of RNA (such as polyadenylated RNA or total RNA), or, on RNA extracted from the same amounts of starting tissue. Such a second sample can also be referred to as a control or standard. Hybridization can also be compared to a second target in the same tissue sample. Experiments can be performed that determine a ratio between the target nucleic acid and a second nucleic acid (a standard or control), e.g., in a normal tissue. When the ratio between the target and control are substantially the same in a normal and sample, the sample is determined or diagnosed not to contain cells. However, if the ratio is different between the normal and sample tissues, the sample is determined to contain cancer cells. The approaches can be combined, and one or more second samples, or second targets can be used. Any second target nucleic acid can be used as a comparison, including "housekeeping" genes, such as beta-actin, alcohol dehydrogenase, or any other gene whose expression does not vary depending upon the disease status of the cell.

Methods of identifying polymorphisms, mutations, etc., of a differentially-regulated gene Polynucleotides of the present invention can also be utilized to identify mutant alleles, SNPs, gene rearrangements and modifications, and other polymorphisms of the wild-type gene. Mutant alleles, polymorphisms, SNPs, etc., can be identified and isolated from cancers that are known, or suspected to have, a genetic component. Identification of such genes can be carried out routinely (see, above for more guidance), e.g., using PCR, hybridization techniques, direct sequencing, mismatch reactions (see, e.g., above), RFLP analysis, SSCP (e.g., Orita et al., *Proc. Natl. Acad. Sci.*, 86:2766, 1992), etc., where a polynucleotide having a sequence selected from Tables 1 and 2 is used as a probe, or genomic sequences thereof. The selected mutant alleles, SNPs, polymorphisms, etc., can be used diagnostically to determine whether a subject has, or is susceptible to a disorder associated with a differentially-regulated gene, as well as to design therapies and predict the outcome of the disorder. Methods involve, e.g., diagnosing a disorder associated with a differentially-regulated gene or determining susceptibility to a disorder, comprising, detecting the presence of a mutation in a gene selected from Tables 1 and 2. The detecting can be carried out by any

effective method, e.g., obtaining cells from a subject, determining the gene sequence or structure of a target gene (using, e.g., mRNA, cDNA, genomic DNA, etc), comparing the sequence or structure of the target gene to the structure of the normal gene, whereby a difference in sequence or structure indicates a mutation in the gene in the subject.

- 5 Polynucleotides can also be used to test for mutations, SNPs, polymorphisms, etc., e.g., using mismatch DNA repair technology as described in U.S. Pat. No. 5,683,877; U.S. Pat. No. 5,656,430; Wu et al., *Proc. Natl. Acad. Sci.*, 89:8779-8783, 1992.

The present invention also relates to methods of detecting polymorphisms in a differentially-regulated gene, comprising, e.g., comparing the structure of: genomic DNA comprising all or part of said gene, mRNA comprising all or part of said gene, cDNA comprising all or part of said gene, or a polypeptide comprising all or part of said gene, with the structure of said gene as set forth herein. The methods can be carried out on a sample from any source, e.g., cells, tissues, body fluids, blood, urine, stool, hair, egg, sperm, etc.

- 15 These methods can be implemented in many different ways. For example, "comparing the structure" steps include, but are not limited to, comparing restriction maps, nucleotide sequences, amino acid sequences, RFLPs, DNase sites, DNA methylation fingerprints (e.g., U.S. Pat. No. 6,214,556), protein cleavage sites, molecular weights, electrophoretic mobilities, charges, ion mobility, etc., between a standard gene and a test gene. The term "structure" can refer to any physical characteristics or configurations which can be used to distinguish between nucleic acids and polypeptides. The methods and instruments used to accomplish the comparing step depends upon the physical characteristics which are to be compared. Thus, various techniques are contemplated, including, e.g., sequencing machines (both amino acid and polynucleotide),
- 25 electrophoresis, mass spectrometer (U.S. Pat. Nos. 6,093,541, 6,002,127), liquid chromatography, HPLC, etc.

To carry out such methods, "all or part" of the gene or polypeptide can be compared. For example, if nucleotide sequencing is utilized, the entire gene can be sequenced, including promoter, introns, and exons, or only parts of it can be sequenced and compared, e.g., exon 1, exon 2, etc.

#### Mutagenesis

Mutated polynucleotide sequences of the present invention are useful for various

- purposes, e.g., to create mutations of the polypeptides they encode, to identify functional regions of genomic DNA, to produce probes for screening libraries, etc. Mutagenesis can be carried out routinely according to any effective method, e.g., oligonucleotide-directed (Smith, M., *Ann. Rev. Genet.* 19:423-463, 1985), degenerate oligonucleotide-directed (Hill et al., *Method Enzymology*, 155:558-568, 1987), region-specific (Myers et al., *Science*, 229:242-246, 1985; Derbyshire et al., *Gene*, 46:145, 1986; Ner et al., *DNA*, 7:127, 1988), linker-scanning (McKnight and Kingsbury, *Science*, 217:316-324, 1982), directed using PCR, recursive ensemble mutagenesis (Arkin and Yourvan, *Proc. Natl. Acad. Sci.*, 89:7811-7815, 1992), random mutagenesis (e.g., U.S. Pat. Nos. 5,096,815; 5,198,346; and 5,223,409), site-directed mutagenesis (e.g., Walder et al., *Gene*, 42:133, 1986; Bauer et al., *Gene*, 37:73, 1985; Craik, *Bio Techniques*, January 1985, 12-19; Smith et al., *Genetic Engineering: Principles and Methods*, Plenum Press, 1981), phage display (e.g., Lowman et al., *Biochem.* 30:10832-10837, 1991; Ladner et al., U.S. Pat. No. 5,223,409; Huse, WIPO Publication WO 92/06204), etc. Desired sequences can also be produced by the assembly of target sequences using mutually priming oligonucleotides (Uhlmann, *Gene*, 71:29-40, 1988). For directed mutagenesis methods, analysis of the three-dimensional structure of a polypeptide can be used to guide and facilitate making mutants which effect polypeptide activity. Sites of substrate-enzyme interaction or other biological activities can also be determined by analysis of crystal structure as determined by such techniques as nuclear magnetic resonance, crystallography or photoaffinity labeling. See, for example, de Vos et al., *Science* 255:306-312, 1992; Smith et al., *J. Mol. Biol.* 224:899-904, 1992; Wlodaver et al., *FEBS Lett.* 309:59-64, 1992.

In addition, libraries of differentially-regulated genes and fragments thereof can be used for screening and selection of gene variants. For instance, a library of coding sequences can be generated by treating a double-stranded DNA with a nuclease under conditions where the nicking occurs, e.g., only once per molecule, denaturing the double-stranded DNA, reannealing it to form double-stranded DNA that can include sense/antisense pairs from different nicked products, removing single-stranded portions from reformed duplexes by treatment with S1 nuclease, and ligating the resulting DNAs into an expression vector. By this method, expression libraries can be made comprising "mutagenized" differentially-regulated genes. The entire coding sequence or parts thereof can be used.



Polynucleotide expression, polypeptides produced thereby, and specific-binding partners thereto.

A polynucleotide according to the present invention can be expressed in a variety of different systems, in vitro and in vivo, according to the desired purpose. For example, a polynucleotide can be inserted into an expression vector, introduced into a desired host, and cultured under conditions effective to achieve expression of a polypeptide coded for by the polynucleotide, to search for specific binding partners. Effective conditions include any culture conditions which are suitable for achieving production of the polypeptide by the host cell, including effective temperatures, pH, medium, additives to the media in which the host cell is cultured (e.g., additives which amplify or induce expression such as butyrate, or methotrexate if the coding polynucleotide is adjacent to a dhfr gene), cycloheximide, cell densities, culture dishes, etc. A polynucleotide can be introduced into the cell by any effective method including, e.g., naked DNA, calcium phosphate precipitation, electroporation, injection, DEAE-Dextran mediated transfection, fusion with liposomes, association with agents which enhance its uptake into cells, viral transfection. A cell into which a polynucleotide of the present invention has been introduced is a transformed host cell. The polynucleotide can be extrachromosomal or integrated into a chromosome(s) of the host cell. It can be stable or transient. An expression vector is selected for its compatibility with the host cell. Host cells include, mammalian cells, e.g., COS, CV1, BHK, CHO, HeLa, LTK, NIH 3T3, PC-3 (CRL-1435), LNCaP (CRL-1740), CA-HPV-10 (CRL-2220), PZ-HPV-7 (CRL-2221), MDA-PCa 2b (CRL-2422), 22Rv1 (CRL2505), NCI-H660 (CRL-5813), HS 804.Sk (CRL-7535), LNCaP-FGF (CRL-10995), RWPE-1 (CRL-11609), RWPE-2 (CRL-11610), PWR-1E (CRL 11611), rat MAT-Ly-LuB-2 (CRL-2376), and other prostate cells, insect cells, such as Sf9 (*S. frugipeda*) and *Drosophila*, bacteria, such as *E. coli*, *Streptococcus*, bacillus, yeast, such as *Saccharomyces*, *S. cerevisiae*, fungal cells, plant cells, embryonic or adult stem cells (e.g., mammalian, such as mouse or human).

Expression control sequences are similarly selected for host compatibility and a desired purpose, e.g., high copy number, high amounts, induction, amplification, controlled expression. Other sequences which can be employed include enhancers such as from SV40, CMV, RSV, inducible promoters, cell-type specific elements, or sequences which allow selective or specific cell expression. Promoters that can be used to drive its expression, include, e.g., the endogenous promoter, MMTV, SV40, trp, lac, tac, or T7 promoters for bacterial hosts; or alpha factor, alcohol oxidase, or PGH promoters for yeast. RNA

promoters can be used to produce RNA transcripts, such as T7 or SP6. See, e.g., Melton et al., *Polynucleotide Res.*, 12(18):7035-7056, 1984; Dunn and Studier, *J. Mol. Bio.*, 166:477-435, 1984; U.S. Pat. No. 5,891,636; Studier et al., *Gene Expression Technology. Methods in Enzymology*, 85:60-89, 1987. In addition, as discussed above, translational signals (including in-frame insertions) can be included.

When a polynucleotide is expressed as a heterologous gene in a transfected cell line, the gene is introduced into a cell as described above, under effective conditions in which the gene is expressed. The term "heterologous" means that the gene has been introduced into the cell line by the "hand-off-man." Introduction of a gene into a cell line is discussed above.

The transfected (or transformed) cell expressing the gene can be lysed or the cell line can be used intact.

For expression and other purposes, a polynucleotide can contain codons found in a naturally-occurring gene, transcript, or cDNA, for example, e.g., as set forth in Tables 1 and 2, or it can contain degenerate codons coding for the same amino acid sequences. For instance, it may be desirable to change the codons in the sequence to optimize the sequence for expression in a desired host. See, e.g., U.S. Pat. Nos. 5,567,600 and 5,567,862.

A polypeptide according to the present invention can be recovered from natural sources, transformed host cells (culture medium or cells) according to the usual methods, including, detergent extraction (e.g., non-ionic detergent, Triton X-100, CHAPS, octylglucoside, Igepal CA-630), ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, hydroxyapatite chromatography, leucin chromatography, gel electrophoresis. Protein refolding steps can be used, as necessary, in completing the configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for purification steps. Another approach is express the polypeptide recombinantly with an affinity tag (Flag epitope, HA epitope, myc epitope, 6xHis, maltose binding protein, chitinase, etc) and then purify by anti-tag antibody-conjugated affinity chromatography.

The present invention also relates to antibodies, and other specific-binding partners, which are specific for polypeptides encoded by polynucleotides of the present invention. Antibodies, e.g., polyclonal, monoclonal, recombinant, chimeric, humanized, single-chain, Fab, and fragments thereof, can be prepared according to any desired method. See, also, screening recombinant immunoglobulin libraries (e.g., Orlandi et al., *Proc. Natl. Acad. Sci.*,

86:3833-3837, 1989; Huse et al., *Science*, 256:1275-1281, 1989; in vitro stimulation of lymphocyte populations; Winter and Milstein, *Nature*, 349: 293-299, 1991. The antibodies can be IgM, IgG, subtypes, IgG2a, IgG1, etc. Antibodies, and immune responses, can also be generated by administering naked DNA. See, e.g., U.S. Pat. Nos. 5,703,055; 5,589,466; 5,580,859. Antibodies can be used from any source, including, goat, rabbit, mouse, chicken (e.g., IgY; see, Duan, WO/029444 for methods of making antibodies in avian hosts, and harvesting the antibodies from the eggs). An antibody specific for a polypeptide means that the antibody recognizes a defined sequence of amino acids within or including the polypeptide. Other specific binding partners include, e.g., aptamers and PNA, can be prepared against specific epitopes or domains of differentially regulated genes.

The preparation of polyclonal antibodies is well-known to those skilled in the art. See, for example, Green et al., *Production of Polyclonal Antisera*, in IMMUNOCHEMICAL PROTOCOLS (Manson, ed.), pages 1-5 (Humana Press 1992); Coligan et al., *Production of Polyclonal Antisera in Rabbits, Rats, Mice and Hamsters*, in CURRENT PROTOCOLS IN IMMUNOLOGY, section 2.4.1 (1992). The preparation of monoclonal antibodies likewise is conventional. See, for example, Kohler & Milstein, *Nature* 256:495 (1975); Coligan et al., sections 2.5.1-2.6.7; and Harlow et al., *ANTIBODIES: A LABORATORY MANUAL*, page 726 (Cold Spring Harbor Pub. 1988).

Antibodies can also be humanized, e.g., where they are to be used therapeutically.

Humanized monoclonal antibodies are produced by transferring mouse complementarity determining regions from heavy and light variable chains of the mouse immunoglobulin into a human variable domain, and then substituting human residues in the framework regions of the murine counterparts. The use of antibody components derived from humanized monoclonal antibodies obviates potential problems associated with the immunogenicity of murine constant regions. General techniques for cloning murine immunoglobulin variable domains are described, for example, by Orlandi et al., *Proc. Nat'l Acad. Sci. USA* 86:3833 (1989), which is hereby incorporated in its entirety by reference. Techniques for producing humanized monoclonal antibodies are described, for example, in U.S. Pat. No. 6,054,297, Jones et al., *Nature* 321: 522 (1986); Riechmann et al., *Nature* 332: 323 (1988); Verhoeyen et al., *Science* 239: 1534 (1988); Carter et al., *Proc. Nat'l Acad. Sci. USA* 89: 4285 (1992); Sandhu, *Crit. Rev. Biotech.* 12: 437 (1992); and Singer et al., *Proc. Nat'l Acad. Sci. USA* 150: 2844 (1993).

Antibodies of the invention also may be derived from human antibody fragments isolated from a combinatorial immunoglobulin library. See, for example, Barbas et al.,

METHODS: A COMPANION TO METHODS IN ENZYMOLOGY, VOL. 2, page 119 (1991); Winter et al., *Ann. Rev. Immunol.* 12: 433 (1994). Cloning and expression vectors that are useful for producing a human immunoglobulin phage library can be obtained commercially, for example, from STRATAGENE Cloning Systems (La Jolla, Calif.).

In addition, antibodies of the present invention may be derived from a human monoclonal antibody. Such antibodies are obtained from transgenic mice that have been "engineered" to produce specific human antibodies in response to antigenic challenge. In this technique, elements of the human heavy and light chain loci are introduced into strains of mice derived from embryonic stem cell lines that contain targeted disruptions of the endogenous heavy and light chain loci. The transgenic mice can synthesize human antibodies specific for human antigens and can be used to produce human antibody-secreting hybridomas. Methods for obtaining human antibodies from transgenic mice are described, e.g., in Green et al., *Nature Genet.* 7:13 (1994); Lonberg et al., *Nature* 368:856 (1994); and Taylor et al., *Int. Immunol.* 6:579 (1994).

Antibody fragments of the present invention can be prepared by proteolytic hydrolysis of the antibody or by expression in *E. coli* of nucleic acid encoding the fragment. Antibody fragments can be obtained by pepsin or papain digestion of whole antibodies by conventional methods. For example, antibody fragments can be produced by enzymatic cleavage of antibodies with pepsin to provide a 5S fragment denoted F(ab')<sub>2</sub>. This fragment can be further cleaved using a thiol reducing agent, and optionally a blocking group for the sulfhydryl groups resulting from cleavage of disulfide linkages, to produce 3.5S Fab' monovalent fragments. Alternatively, an enzymatic cleavage using pepsin produces two monovalent Fab' fragments and an Fc fragment directly. These methods are described, for example, by Goldenberg, U.S. Pat. No. 4,036,945 and No. 4,331,647, and references contained therein. These patents are hereby incorporated in their entireties by reference. See also Nisioihoff et al., *Arch. Biochem. Biophys.* 89:230 (1960); Porter, *Biochem. J.* 73:119 (1959); Edelman et al., *METHODS IN ENZYMOLOGY*, VOL. 1, page 422 (Academic Press 1967); and Coligan et al. at sections 2.8.1-2.8.10 and 2.10.1-2.10.4.

Other methods of cleaving antibodies, such as separation of heavy chains to form monovalent light-heavy chain fragments, further cleavage of fragments, or other enzymatic, chemical, or genetic techniques can also be used. For example, Fv fragments comprise an association of V<sub>sub H</sub> and V<sub>sub L</sub> chains. This association may be noncovalent, as described in Inbar et al., *Proc. Nat'l Acad. Sci. USA* 69:2659 (1972). Alternatively, the

variable chains can be linked by an intermolecular disulfide bond or cross-linked by chemicals such as glutaraldehyde. See, e.g., Sandhu, supra. Preferably, the Fv fragments comprise V.sub.H and V.sub.L chains connected by a peptide linker. These single-chain antigen binding proteins (sFv) are prepared by constructing a structural gene comprising nucleic acid sequences encoding the V.sub.H and V.sub.L domains connected by an oligonucleotide. The structural gene is inserted into an expression vector, which is subsequently introduced into a host cell such as E. coli. The recombinant host cells synthesize a single polypeptide chain with a linker peptide bridging the two V domains. Methods for producing sFvs are described, for example, by Whitlow et al., METHODS: A COMPANION TO METHODS IN ENZYMOLOGY, VOL. 2, page 97 (1991); Bird et al., Science 242:423-426 (1988); Ladner et al., U.S. Pat. No. 4,946,778; Pack et al., Bio/Technology 11: 1271-77 (1993); and Sandhu, supra.

Another form of an antibody fragment is a peptide coding for a single

complementarity-determining region (CDR). CDR peptides ("minimal recognition units") can be obtained by constructing genes encoding the CDR of an antibody of interest. Such genes are prepared, for example, by using the polymerase chain reaction to synthesize the variable region from RNA of antibody-producing cells. See, for example, Larrick et al., METHODS: A COMPANION TO METHODS IN ENZYMOLOGY, VOL. 2, page 106 (1991).

The term "antibody" as used herein includes intact molecules as well as fragments thereof, such as Fab, F(ab')<sub>2</sub>, and Fv which are capable of binding to an epitopic determinant present in Bin1 polypeptide. Such antibody fragments retain some ability to selectively bind with its antigen or receptor. The term "epitope" refers to an antigenic determinant on an antigen to which the paratope of an antibody binds. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. Antibodies can be prepared against specific epitopes or polypeptide domains.

Antibodies which bind to a differentially-regulated polypeptide of the present invention can be prepared using an intact polypeptide or fragments containing small peptides of interest as the immunizing antigen. For example, it may be desirable to produce antibodies that specifically bind to the N- or C-terminal domains of said polypeptide. The polypeptide or peptide used to immunize an animal which is derived from translated cDNA or chemically synthesized which can be conjugated to a carrier protein, if desired. Such commonly used

carriers which are chemically coupled to the immunizing peptide include keyhole limpet hemocyanin (KLH), thyroglobulin, bovine serum albumin (BSA), and tetanus toxoid.

Polyclonal or monoclonal antibodies can be further purified, for example, by binding to and elution from a matrix to which the polypeptide or a peptide to which the antibodies were raised is bound. Those of skill in the art will know of various techniques common in the immunology arts for purification and/or concentration of polyclonal antibodies, as well as monoclonal antibodies (See for example, Coligan, et al., Unit 9, *Current Protocols in Immunology*, Wiley Interscience, 1994, incorporated by reference).

Anti-idiotypic technology can also be used to produce invention monoclonal

antibodies which mimic an epitope. For example, an anti-idiotypic monoclonal antibody made to a first monoclonal antibody will have a binding domain in the hypervariable region which is the "image" of the epitope bound by the first monoclonal antibody.

Methods of detecting polypeptides

Polypeptides coded for by a differentially-regulated gene of the present invention can be detected, visualized, determined, quantitated, etc. according to any effective method. Useful methods include, e.g., but are not limited to, immunoassays, RIA (radioimmunoassay), ELISA, (enzyme-linked-immunosorbent assay), immunofluorescence, flow cytometry, histology, electron microscopy, light microscopy, in situ assays, immunoprecipitation, Western blot, etc.

Immunoassays may be carried in liquid or on biological support. For instance, a sample (e.g., blood, stool, urine, cells, tissue, body fluids, etc.) can be brought in contact with and immobilized onto a solid phase support or carrier such as nitrocellulose, or other solid support that is capable of immobilizing cells, cell particles or soluble proteins. The support may then be washed with suitable buffers followed by treatment with the detectably labeled differentially-regulated gene specific antibody. The solid phase support can then be washed with a buffer a second time to remove unbound antibody. The amount of bound label on solid support may then be detected by conventional means.

A "solid phase support or carrier" includes any support capable of binding an antigen, antibody, or other specific binding partner. Supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, and magnetite. A support material can have any structural or physical configuration. Thus, the support configuration may be spherical, as in a bead, or cylindrical,

as in the inside surface of a test tube, or the external surface of a rod. Alternatively, the surface may be flat such as a sheet, test strip, etc. Preferred supports include polystyrene beads

One of the many ways in which gene peptide-specific antibody can be detectably labeled is by linking it to an enzyme and using it in an enzyme immunoassay (EIA). See, e.g., Voller, A., "The Enzyme Linked Immunosorbent Assay (ELISA)," 1978, Diagnostic Horizons 2, 1-7, Microbiological Associates Quarterly Publication, Walkersville, Md.); Voller, A. et al., 1978, J. Clin. Pathol. 31, 507-520; Butler, J. E., 1981, Meth. Enzymol. 73, 482-523; Maggio, E. (ed.), 1980, Enzyme Immunoassay, CRC Press, Boca Raton, Fla. The enzyme which is bound to the antibody will react with an appropriate substrate, preferably a chromogenic substrate, in such a manner as to produce a chemical moiety that can be detected, for example, by spectrophotometric, fluorimetric or by visual means. Enzymes that can be used to detectably label the antibody include, but are not limited to, malate dehydrogenase, staphylococcal nuclease, delta-5-steroid isomerase, yeast alcohol dehydrogenase, alpha-glycerophosphate, dehydrogenase, triose phosphate isomerase, horseradish peroxidase, alkaline phosphatase, asparaginase, glucose oxidase, beta-galactosidase, ribonuclease, urease, catalase, glucose-6-phosphate dehydrogenase, glucoamylase and acetylcholinesterase. The detection can be accomplished by colorimetric methods that employ a chromogenic substrate for the enzyme. Detection may also be accomplished by visual comparison of the extent of enzymatic reaction of a substrate in comparison with similarly prepared standards.

Detection may also be accomplished using any of a variety of other immunoassays. For example, by radioactively labeling the antibodies or antibody fragments, it is possible to detect differentially-regulated peptides through the use of a radioimmunoassay (RIA). See, e.g., Weintraub, B., Principles of Radioimmunoassays, Seventh Training Course on Radioligand Assay Techniques, The Endocrine Society, March, 1986. The radioactive isotope can be detected by such means as the use of a gamma counter or a scintillation counter or by autoradiography.

It is also possible to label the antibody with a fluorescent compound. When the fluorescently labeled antibody is exposed to light of the proper wave length, its presence can then be detected due to fluorescence. Among the most commonly used fluorescent labeling compounds are fluorescein isothiocyanate, rhodamine, phycoerythrin, phycocyanin, allophycocyanin, o-phthalaldehyde and fluorescamine. The antibody can also be detectably

labeled using fluorescence emitting metals such as those in the lanthanide series. These metals can be attached to the antibody using such metal chelating groups as diethylenetriaminepentaacetic acid (DTPA) or ethylenediaminetetraacetic acid (EDTA).

The antibody also can be detectably labeled by coupling it to a chemiluminescent compound. The presence of the chemiluminescent-tagged antibody is then determined by detecting the presence of luminescence that arises during the course of a chemical reaction. Examples of useful chemiluminescent labeling compounds are luminol, isoluminol, theromatic acridinium ester, imidazole, acridinium salt and oxalate ester.

Likewise, a bioluminescent compound may be used to label the antibody of the present invention. Bioluminescence is a type of chemiluminescence found in biological systems in which a catalytic protein increases the efficiency of the chemiluminescent reaction. The presence of a bioluminescent protein is determined by detecting the presence of luminescence. Important bioluminescent compounds for purposes of labeling are luciferin, luciferase and aequorin.

#### Tissue and Disease

The prostate is a secretory organ surrounding the neck of the bladder and urethra. Its primary function is to produce fluids and other materials necessary for sperm transport and maintenance. Structurally, it has both glandular and nonglandular components. The glandular component is predominantly comprised of ducts and acini responsible for the production and transport prostatic fluids. Epithelial cells are the main identifiable cell found in these regions, primarily of the basal and secretory types, but also endocrine-paracrine and transitional epithelial. The non-glandular component contains the capsular and muscle tissues, which, respectively, hold the organ together and function in fluid discharge. See, e.g., Histology for Pathologists, Sternberg, S.S., editor, Raven Press, NY, 1992, Chapter 40.

The major diseases of the prostate include, e.g., prostatic hyperplasia (BPH), prostatitis, and prostatic cancer (e.g., prostatic adenocarcinoma). BPH is a benign, proliferative disease of the prostatic epithelial cells. While it may cause urinary tract obstruction in some patients, for the most part, it is generally asymptomatic. Prostatic cancer, on the other hand, is the most common form of cancer in white males in the United States, occurring predominantly in males over age 50. The prevalence of prostate diseases, such as prostate cancer, has made the discovery of prostate selective markers and gene expression patterns of great importance.

The most common scale of assessing prostate pathology is the Gleason grading system. See, e.g., Bostwick, *Am. J. Clin. Path.*, 102: s38-s56, 1994. Once the cancer is identified, staging can assess the size, location, and extent of the cancer. Several different staging scales are commonly used, including stages A-D, and Tumor-Nodes-Metastases (TNM). For treatment, diagnosis, staging, etc., of prostate conditions, methods can be carried out analogously to, and in combination with, U.S. Pat. Nos. 6,107,090; 6,057,116; 6,034,218; 6,004,267; 5,919,638; 5,882,864; 5,763,202; 5,747,264; 5,688,649; 5,552,277.

In addition, the present invention relates to methods of assessing a therapeutic or preventative intervention in a subject having a prostate cancer, comprising, e.g., detecting the expression levels of differentially-regulated target genes, wherein the target genes comprise a gene which is represented by a sequence selected from Tables 1 and 2, or, a gene represented by a sequence having 95% sequence identity or more to a sequence selected from Tables 1 and 2. By "therapeutic or preventative intervention," it is meant, e.g., a drug administered a patient, surgery, radiation, chemotherapy, and other measures taken to prevent a cancer or treat a cancer.

Grading, staging, comparing, assessing, methods and compositions

The present invention also relates to methods and compositions for staging and grading cancers. As already defined, staging relates to determining the extent of a cancer's spread, including its size and the degree to which other tissues, such as lymph nodes are involved in the cancer. Grading refers to the degree of a cell's retention of the characteristics of the tissue of its origin. A lower grade cancer comprises tumor cells that more closely resemble normal cells than a medium or higher grade cancer. Grading can be a useful diagnostic and prognostic tool. Higher grade cancers usually behave more aggressively than lower grade cancers. Thus, knowledge of the cancer grade, as well as its stage, can be a significant factor in the choice of the appropriate therapeutic intervention for the particular patient, e.g., surgery, radiation, chemotherapy, etc. Staging and grading can also be used in conjunction with a therapy to assess its efficacy, to determine prognosis, to determine effective dosages, etc.

Various methods of staging and grading cancers can be employed in accordance with the present invention. A "cell expression profile" or "cell expression fingerprint" is a representation of the expression of various different genes (e.g., polynucleotide sequences of SEQ ID NOS 1-107) in a given cell or sample comprising cells. These cell expression

profiles can be useful as reference standards. The cell expression fingerprints can be used alone for grading, or in combination with other grading methods.

The present invention also relates to methods and compositions for diagnosing a prostate cancer, or determining susceptibility to a prostate cancer, using polynucleotides, polypeptides, and specific-binding partners of the present invention to detect, assess, determine, etc., differentially-regulated genes of the present invention. In such methods, the gene can serve as a marker for prostate cancer, e.g., where the gene, when mutant, is a direct cause of the prostate cancer; where the gene is affected by another gene(s) which is directly responsible for the prostate cancer, e.g., when the gene is part of the same signaling pathway as the directly responsible gene; and, where the gene is chromosomally linked to the gene(s) directly responsible for the prostate cancer, and segregates with it. Many other situations are possible. To detect, assess, determine, etc., a probe specific for the gene can be employed as described above and below. Any method of detecting and/or assessing the gene can be used, including detecting expression of the gene using polynucleotides, antibodies, or other specific-binding partners.

The present invention relates to methods of diagnosing a disorder associated with prostate cancer, or determining a subject's susceptibility to such prostate cancer, comprising, e.g., assessing the expression of a differentially-regulated gene in a tissue sample comprising tissue or cells suspected of having prostate cancer (e.g., where the sample comprises prostate). The phrase "diagnosing" indicates that it is determined whether the sample has a prostate cancer cells. "Determining a subject's susceptibility to a prostate cancer" indicates that the subject is assessed for whether s/he is predisposed to get such a disease or disorder, where the predisposition is indicated by abnormal expression of the gene (e.g., gene mutation, gene expression pattern is not normal, etc.). Predisposition or susceptibility to a disease may result when a such disease is influenced by epigenetic, environmental, etc., factors.

By the phrase "assessing expression of a differentially-regulated gene," it is meant that the functional status of the gene is evaluated. This includes, but is not limited to, measuring expression levels of said gene, determining the genomic structure of said gene, determining the mRNA structure of transcripts from said gene, or measuring the expression levels of polypeptide coded for by said gene. Thus, the term "assessing expression" includes evaluating the all aspects of the transcriptional and translational machinery of the gene. For instance, if a promoter defect causes, or is suspected of

causing the disorder, then a sample can be evaluated (i.e., "assessed") by looking (e.g., sequencing or restriction mapping) at the promoter sequence in the gene, by detecting transcription products (e.g., RNA), by detecting translation product (e.g., polypeptide). Any measure of whether the gene is functional can be used, including, polypeptide, polynucleotide, and functional assays for the gene's biological activity.

In making the assessment, it can be useful to compare the results to a normal gene, e.g., a gene which is not associated with the disorder. The nature of the comparison can be determined routinely, depending upon how the assessing is accomplished. If, for example, the mRNA levels of a sample is detected, then the mRNA levels of a normal can serve as a comparison, or a gene which is known not to be affected by the disorder.

Methods of detecting mRNA are well known, and discussed above, e.g., but not limited to, Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, etc. Similarly, if polypeptide production is used to evaluate the gene, then the polypeptide in a normal tissue sample can be used as a comparison, or, polypeptide from a different gene whose expression is known not to be affected by the disorder. These are only examples of how such a method could be carried out.

Assessing the effects of therapeutic and preventative interventions (e.g., administration of a drug, chemotherapy, radiation, etc.) on prostate cancer is a major effort in drug discovery, clinical medicine, and pharmacogenomics. The evaluation of therapeutic and preventative measures, whether experimental or already in clinical use, has broad applicability, e.g., in clinical trials, for monitoring the status of a patient, for analyzing and assessing animal models, and in any scenario involving cancer treatment and prevention. Analyzing the expression profiles of polynucleotides of the present invention can be utilized as a parameter by which interventions are judged and measured. Treatment of a disorder can change the expression profile in some manner which is prognostic or indicative of the drug's effect on it. Changes in the profile can indicate, e.g., drug toxicity, return to a normal level, etc. Accordingly, the present invention also relates to methods of monitoring or assessing a therapeutic or preventative measure (e.g., chemotherapy, radiation, anti-neoplastic drugs, antibodies, etc.) in a subject having prostate cancer, or, susceptible to such a disorder, comprising, e.g., detecting the expression levels of one or more differentially-regulated genes of the present invention. A subject can be a cell-based assay system, non-human animal model, human patient, etc. Detecting can be accomplished as described for the methods above and below. By

"therapeutic or preventative intervention," it is meant, e.g., a drug administered to a patient, surgery, radiation, chemotherapy, and other measures taken to prevent, treat, or diagnose prostate cancer.

Expression can be assessed in any sample comprising any tissue or cell type, body fluid, etc., as discussed for other methods of the present invention, including cells from prostate can be used, or cells derived from prostate. By the phrase "cells derived from prostate," it is meant that the derived cells originate from prostate, e.g., when metastasis from a primary tumor site has occurred, when a progenitor-type or pluripotent cell gives rise to other cells, etc.

#### Identifying agent methods

The present invention also relates to methods of identifying agents, and the agents themselves, which modulate prostate cancer genes. These agents can be used to modulate the biological activity of the polypeptide encoded for the gene, or the gene, itself. Agents which regulate the gene or its product are useful in variety of different environments, including as medicinal agents to treat or prevent disorders associated with prostate cancer genes and as research reagents to modify the function of tissues and cell.

Methods of identifying agents generally comprise steps in which an agent is placed in contact with the gene, transcription product, translation product, or other target, and then a determination is performed to assess whether the agent "modulates" the target. The specific method utilized will depend upon a number of factors, including, e.g., the target (i.e., is it the gene or polypeptide encoded by it), the environment (e.g., in vitro or in vivo), the composition of the agent, etc.

For modulating the expression of a prostate cancer gene, a method can comprise, in any effective order, one or more of the following steps, e.g., contacting a prostate cancer gene (e.g., in a cell population) with a test agent under conditions effective for said test agent to modulate the expression of the prostate cancer, and determining whether said test agent modulates said gene. An agent can modulate expression of a gene at any level, including transcription, translation, and/or perdurance of the nucleic acid (e.g., degradation, stability, etc.) in the cell. For modulating the biological activity of prostate cancer polypeptides, a method can comprise, in any effective order, one or more of the following steps, e.g., contacting a polypeptide (e.g., in a cell, lysate, or isolated) with a test agent under conditions

effective for said test agent to modulate the biological activity of said polypeptide, and determining whether said test agent modulates said biological activity.

Contacting a gene or polypeptide with the test agent can be accomplished by any suitable method and/or means that places the agent in a position to functionally control its expression or biological activity. Functional control indicates that the agent can exert its physiological effect on the gene or polypeptide through whatever mechanism it works. The choice of the method and/or means can depend upon the nature of the agent and the condition and type of environment in which the gene or polypeptide is presented, e.g., lysate, isolated, or in a cell population (such as, *in vivo*, *in vitro*, organ explants, etc.). For instance, if the cell population is an *in vitro* cell culture, the agent can be contacted with the cells by adding it directly into the culture medium. If the agent cannot dissolve readily in an aqueous medium, it can be incorporated into liposomes, or another lipophilic carrier, and then administered to the cell culture. Contact can also be facilitated by incorporation of agent with carriers and delivery molecules and complexes, by injection, by infusion, etc.

After the agent has been administered in such a way that it can gain access to the gene or polypeptide, it can be determined whether the test agent modulates the gene or polypeptide expression or biological activity. Modulation can be of any type, quality, or quantity, e.g., increase, facilitate, enhance, up-regulate, stimulate, activate, amplify, augment, induce, decrease, down-regulate, diminish, lessen, reduce, etc. The modulatory quantity can also encompass any value, e.g., 1%, 5%, 10%, 50%, 75%, 1-fold, 2-fold, 5-fold, 10-fold, 100-fold, etc. To modulate gene expression means, e.g., that the test agent has an effect on its expression, e.g., to effect the amount of transcription, to effect RNA splicing, to effect translation of the RNA into polypeptide, to effect RNA or polypeptide stability, to effect polyadenylation or other processing of the RNA, to effect post-transcriptional or post-translational processing, etc. To modulate biological activity means, e.g., that a functional activity of the polypeptide is changed in comparison to its normal activity in the absence of the agent. This effect includes, increase, decrease, block, inhibit, enhance, etc.

A test agent can be of any molecular composition, e.g., chemical compounds, biomolecules, such as polypeptides, lipids, nucleic acids (e.g., antisense to a polynucleotide sequence selected from Tables 1 and 2, or genomic sequences thereof), carbohydrates, antibodies, ribozymes, double-stranded RNA, aptamers, etc. For example, if a polypeptide to be modulated is a cell-surface molecule, a test agent can be an antibody that specifically recognizes it and, e.g., causes the polypeptide to be internalized, leading to its down

regulation on the surface of the cell. Such an effect does not have to be permanent, but can require the presence of the antibody to continue the down-regulatory effect. Antibodies can also be used to modulate the biological activity a polypeptide in a lysate or other cell-free form. Antisense can also be used as test agents to modulate gene expression.

## Markers

The polynucleotides of the present invention can be used with other markers, especially prostate and prostate cancer markers to identify, detect, stage, diagnosis, determine, prognosticate, treat, etc., tissue, diseases and conditions, etc, of the prostate. Markers can be polynucleotides, polypeptides, antibodies, ligands, specific binding partners, etc.

A number of genes and gene products have been identified which are associated with prostate cancer metastasis and/or progression, e.g., PSA, KAI1 (shows decreased expression in metastatic cells; Dong et al., *Science*, 268:884-6, 1995), D44 isoforms (differentially-regulated during carcinoma progression; Noordzij et al., *Clin. Cancer Res.*, 3:805-15, 1997), p53 (Effert et al., *J. Urol.*, 150:257-61, 1993), Rb, CDKN2, E-cadherin, PTEN (Hamilton et al., *Br. J. Cancer*, 82:1671-6, 2000; Dong et al., *Clin. Cancer Res.*, 7:304-308, 2001), bcl-2, prostatic acid phosphatase (PAP), prostate specific membrane antigen (e.g., U.S. Pat. Nos. 5,538,866 and 6,107,090), Smad3 (e.g., Kang et al., *Proc. Natl. Acad. Sci.*, 98:3018-3023, 2001), TGF-beta, and other oncogenes and tumor suppressor genes. See, also, Myers and Grizzle, *Eur. Urol.*, 30:153-166, 1996, for other biomarkers associated with prostatic carcinoma, such as PCNA, p185-erbB-2, p180erbB-3, TAG-72, nm23-H1 and FASE. Such markers can be used in combination with the methods of the present invention to facilitate identifying, grading, staging, prognostication, etc, of conditions and diseases of the prostate.

## Therapeutics

Selective polynucleotides, polypeptides, and specific-binding partners thereto, can be utilized in therapeutic applications, especially to treat prostate cancer. Useful methods include, but are not limited to, immunotherapy (e.g., using specific-binding partners to polypeptides), vaccination (e.g., using a selective polypeptide or a naked DNA encoding such polypeptide), protein or polypeptide replacement therapy, gene therapy (e.g., germ-line correction, antisense), etc.

Various immunotherapeutic approaches can be used. For instance, unlabeled

antibody that specifically recognizes a tissue-specific antigen can be used to stimulate the body to destroy or attack the cancer, to cause down-regulation, to produce complement-mediated lysis, to inhibit cell growth, etc., of target cells which display the antigen, e.g., analogously to how c-erbB-2 antibodies are used to treat breast cancer. In addition, antibody can be labeled or conjugated to enhance its deleterious effect, e.g., with radionuclides and other energy emitting entities, toxins, such as ricin, exotoxin A (ETA), and diphtheria, cytotoxic or cytostatic agents, immunomodulators, chemotherapeutic agents, etc. See, e.g., U.S. Pat. No. 6,107,090.

An antibody or other specific-binding partner can be conjugated to a second molecule, such as a cytotoxic agent, and used for targeting the second molecule to a tissue-antigen positive cell (Violetta, E. S. et al., 1993, Immunotoxin therapy, in DeVita, Jr., V. T. et al., eds, Cancer: Principles and Practice of Oncology, 4th ed., J. B. Lippincott Co., Philadelphia, 2624-2636). Examples of cytotoxic agents include, but are not limited to, antimetabolites, alkylating agents, anthracyclines, antibiotics, anti-mitotic agents, radioisotopes and chemotherapeutic agents. Further examples of cytotoxic agents include, but are not limited to ricin, doxorubicin, daunorubicin, taxol, etidonium bromide, mitomycin, etoposide, teniposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, 1-dehydrotestosterone, diphtheria toxin, Pseudomonas exotoxin (PE) A, PE40, abrin, elongation factor-2 and glucocorticoid. Techniques for conjugating therapeutic agents to antibodies are well.

In addition to immunotherapy, polynucleotides and polypeptides can be used as targets for non-immunotherapeutic applications, e.g., using compounds which interfere with function, expression (e.g., antisense as a therapeutic agent), assembly, etc. RNA interference can be used *in vitro* and *in vivo* to silence differentially-expressed genes when its expression contributes to a disease (but also for other purposes, e.g., to identify the gene's function to change a developmental pathway of a cell, etc.). See, e.g., Sharp and Zamore, *Science*, 287:2431-2433, 2001; Grishok et al., *Science*, 287:2494, 2001.

Delivery of therapeutic agents can be achieved according to any effective method, including, liposomes, viruses, plasmid vectors, bacterial delivery systems, orally, systemically, etc. Therapeutic agents of the present invention can be administered in any form by any effective route, including, e.g., oral, parenteral, enteral, intraperitoneal, topical, transdermal (e.g., using any standard patch), ophthalmic, nasally, local, non-oral, such as aerosol, inhalation, subcutaneous, intramuscular, buccal, sublingual, rectal, vaginal, intra-

arterial, and intrathecal, etc. They can be administered alone, or in combination with any ingredient(s), active or inactive.

In addition to therapeutics, *per se*, the present invention also relates to methods of treating prostate cancer showing altered expression of differentially-regulated genes, such as Tables 1 and 2, comprising, e.g., administering to a subject in need thereof a therapeutic agent which is effective for regulating expression of said genes and/or which is effective in treating said disease. The term "treating" is used conventionally, e.g., the management or care of a subject for the purpose of combating, alleviating, reducing, relieving, improving the condition of, etc., of a disease or disorder. By the phrase "altered expression," it is meant that the disease is associated with a mutation in the gene, or any modification to the gene (or corresponding product) which affects its normal function. Thus, expression of a differentially-regulated gene refers to, e.g., transcription, translation, splicing, stability of the mRNA or protein product, activity of the gene product, differential expression, etc.

Any agent which "treats" the disease can be used. Such an agent can be one which regulates the expression of the gene. Expression refers to the same acts already mentioned, e.g. transcription, translation, splicing, stability of the mRNA or protein product, activity of the gene product, differential expression, etc. For instance, if the condition was a result of a complete deficiency of the gene product, administration of gene product to a patient would be said to treat the disease and regulate the gene's expression. Many other possible situations are possible, e.g., where the gene is aberrantly expressed, and the therapeutic agent regulates the aberrant expression by restoring its normal expression pattern.

## 25 Antisense

Antisense polynucleotide (e.g., RNA) can also be prepared from a polynucleotide according to the present invention, preferably an anti-sense to a gene of Tables 1 and 2. Antisense polynucleotide can be used in various ways, such as to regulate or modulate expression of the polypeptides they encode, e.g., inhibit their expression, for *in situ* hybridization, for therapeutic purposes, for making targeted mutations (*in vivo*, triplex, etc.) etc. For guidance on administering and designing anti-sense, see, e.g., U.S. Pat. Nos. 6,200,960, 6,200,807, 6,197,584, 6,190,869, 6,190,661, 6,187,587, 6,168,950, 6,153,595, 6,150,162, 6,133,246, 6,117,847, 6,096,722, 6,087,343, 6,040,296, 6,005,095, 5,998,383,



5,994,230, 5,891,725, 5,885,970, and 5,840,708. An antisense polynucleotides can be operably linked to an expression control sequence. A total length of about 35 bp can be used in cell culture with cationic liposomes to facilitate cellular uptake, but for *in vivo* use, preferably shorter oligonucleotides are administered, e.g. 25 nucleotides.

Antisense polynucleotides can comprise modified, nonnaturally-occurring nucleotides and linkages between the nucleotides (e.g., modification of the phosphate-sugar backbone; methyl phosphonate, phosphorothioate, or phosphorodithioate linkages; and 2'-O-methyl ribose sugar units) e.g., to enhance *in vivo* or *in vitro* stability, to confer nuclease resistance, to modulate uptake, to modulate cellular distribution and compartmentalization, etc. Any

effective nucleotide or modification can be used, including those already mentioned, as known in the art, etc., e.g., disclosed in U.S. Pat. Nos. 6,133,438; 6,127,533; 6,124,445; 6,121,437; 5,218,103 (e.g., nucleoside thiophosphoramidites); 4,973,679; Sproat et al., "2'-O-

Methyloligoribonucleotides: synthesis and applications," Oligonucleotides and Analogs A Practical Approach, Eckstein (ed.), IRL Press, Oxford, 1991, 49-86; Iribarren et al., "2'-O-

Alkyl Oligoribonucleotides as Antisense Probes," Proc. Natl. Acad. Sci. USA, 1990, 87, 7747-7751; Cotton et al., "2'-O-methyl, 2'-O-ethyl oligoribonucleotides and phosphorothioate oligodeoxyribonucleotides as inhibitors of the *in vitro* U7 snRNP-dependent mRNA processing event," Nucl. Acids Res., 1991, 19, 2629-2635.

## 20 Arrays

The present invention also relates to an ordered array of polynucleotide probes and specific-binding partners (e.g., antibodies) for detecting the expression of differentially-regulated genes in a sample, comprising, one or more polynucleotide probes or specific binding partners associated with a solid support, wherein each probe is specific for said genes, and the probes comprise a nucleotide sequence of Tables 1 and 2 which is specific for said gene, a nucleotide sequence having sequence identity to Tables 1 and 2 which is specific for said gene or polynucleotide, or complements thereto, or a specific-binding partner which is specific for said genes.

The phrase "ordered array" indicates that the probes are arranged in an identifiable or position-addressable pattern, e.g., such as the arrays disclosed in U.S. Pat. Nos. 6,156,501, 6,077,673, 6,054,270, 5,723,320, 5,700,637, WO09919711, WO000223803. The probes are associated with the solid support in any effective way. For instance, the probes can be bound to the solid support, either by polymerizing the probes on the substrate, or by attaching a

probe to the substrate. Association can be, covalent, electrostatic, noncovalent, hydrophobic, hydrophilic, noncovalent, coordination, adsorbed, absorbed, polar, etc. When fibers or hollow filaments are utilized for the array, the probes can fill the hollow orifice, be absorbed into the solid filament, be attached to the surface of the orifice, etc. Probes can be of any effective size, sequence identity, composition, etc., as already discussed.

Ordered arrays can further comprise polynucleotide probes or specific-binding partners which are specific for other genes, including genes specific for prostate or disorders associated with prostate, such as prostate cancer.

## 10 Transgenic animals

The present invention also relates to transgenic animals comprising differentially-regulated genes of the present invention. Such genes, as discussed in more detail below, include, but are not limited to, functionally-disrupted genes, mutated genes, ectopically or selectively-expressed genes, inducible or regulatable genes, etc. These transgenic animals can be produced according to any suitable technique or method, including homologous recombination, mutagenesis (e.g., ENU, Rathkolb et al., *Exp. Physiol.*, 85(6):635-644, 2000), and the tetracycline-regulated gene expression system (e.g., U.S. Pat. No. 6,242,667). The term "gene" as used herein includes any part of a gene, i.e., regulatory sequences, promoters, enhancers, exons, introns, coding sequences, etc. The nucleic acid present in the construct or transgene can be naturally-occurring wild-type, polymorphic, or mutated.

Along these lines, polynucleotides of the present invention can be used to create transgenic animals, e.g. a non-human animal, comprising at least one cell whose genome comprises a functional disruption of a differentially-regulated gene. By the phrases "functional disruption" or "functionally disrupted," it is meant that the gene does not express a biologically-active product. It can be substantially deficient in at least one functional activity coded for by the gene. Expression of a polypeptide can be substantially absent, i.e., essentially undetectable amounts are made. However, polypeptide can also be made, but which is deficient in activity, e.g., where only an amino-terminal portion of the gene product is produced.

The transgenic animal can comprise one or more cells. When substantially all its cells contain the engineered gene, it can be referred to as a transgenic animal "whose genome comprises" the engineered gene. This indicates that the endogenous gene loci of the animal has been modified and substantially all cells contain such modification.

Functional disruption of the gene can be accomplished in any effective way, including, e.g., introduction of a stop codon into any part of the coding sequence such that the resulting polypeptide is biologically inactive (e.g., because it lacks a catalytic domain, a ligand binding domain, etc.), introduction of a mutation into a promoter or other regulatory sequence that is effective to turn it off, or reduce transcription of the gene, insertion of an exogenous sequence into the gene which inactivates it (e.g., which disrupts the production of a biologically-active polypeptide or which disrupts the promoter or other transcriptional machinery), deletion of sequences from the a differentially-regulated gene, etc. Examples of transgenic animals having functionally disrupted genes are well known, e.g., as described in U.S. Pat. Nos. 6,239,326, 6,225,525, 6,207,878, 6,194,633, 6,187,992, 6,180,849, 6,177,610, 6,100,445, 6,087,555, 6,080,910, 6,069,297, 6,060,642, 6,028,244, 6,013,858, 5,981,830, 5,866,760, 5,859,314, 5,850,004, 5,817,912, 5,789,654, 5,777,195, and 5,569,824. A transgenic animal which comprises the functional disruption can also be referred to as a "knock-out" animal, since the biological activity of its a differentially-regulated gene has been "knocked-out." Knock-outs can be homozygous or heterozygous.

For creating functional disrupted genes, and other gene mutations, homologous recombination technology is of special interest since it allows specific regions of the genome to be targeted. Using homologous recombination methods, genes can be specifically-inactivated, specific mutations can be introduced, and exogenous sequences can be introduced at specific sites. These methods are well known in the art, e.g., as described in the patents above. See, also, Robertson, *Biol. Reproduc.*, 44(2):238-245, 1991. Generally, the genetic engineering is performed in an embryonic stem (ES) cell, or other pluripotent cell line (e.g., adult stem cells, EG cells), and that genetically-modified cell (or nucleus) is used to create a whole organism. Nuclear transfer can be used in combination with homologous recombination technologies.

For example, a differentially-regulated gene locus can be disrupted in mouse ES cells using a positive-negative selection method (e.g., Mansour et al., *Nature*, 336:348-352, 1988). In this method, a targeting vector can be constructed which comprises a part of the gene to be targeted. A selectable marker, such as neomycin resistance genes, can be inserted into a differentially-regulated gene exon present in the targeting vector, disrupting it. When the vector recombines with the ES cell genome, it disrupts the function of the gene. The presence in the cell of the vector can be determined by expression of neomycin resistance. See, e.g., U.S. Pat. No. 6,239,326. Cells having at least one functionally disrupted gene can

be used to make chimeric and germline animals, e.g., animals having somatic and/or germ cells comprising the engineered gene. Homozygous knock-out animals can be obtained from breeding heterozygous knock-out animals. See, e.g., U.S. Pat. No. 6,225,525.

A transgenic animal, or animal cell, lacking one or more functional differentially-regulated genes can be useful in a variety of applications, including, as an animal model for cancer, for drug screening assays, as a source of tissues deficient in said gene activity, and any of the utilities mentioned in any issued U.S. Patent on transgenic animals, including, U.S. Pat. Nos. 6,239,326, 6,225,525, 6,207,878, 6,194,633, 6,187,992, 6,180,849, 6,177,610, 6,100,445, 6,087,555, 6,080,910, 6,069,297, 6,060,642, 6,028,244, 6,013,858, 5,981,830, 5,866,760, 5,859,314, 5,850,004, 5,817,912, 5,789,654, 5,777,195, and 5,569,824.

The present invention also relates to non-human, transgenic animal whose genome comprises recombinant a differentially-regulated gene nucleic acid operatively linked to an expression control sequence effective to express said coding sequence, e.g., in prostate. such a transgenic animal can also be referred to as a "knock-in" animal since an exogenous gene has been introduced, stably, into its genome.

A recombinant a differentially-regulated gene nucleic acid refers to a gene which has been introduced into a target host cell and optionally modified, such as cells derived from animals, plants, bacteria, yeast, etc. A recombinant a differentially-regulated gene includes completely synthetic nucleic acid sequences, semi-synthetic nucleic acid sequences, sequences derived from natural sources, and chimeras thereof. "Operable linkage" has the meaning used through the specification, i.e., placed in a functional relationship with another nucleic acid. When a gene is operably linked to an expression control sequence, as explained above, it indicates that the gene (e.g., coding sequence) is joined to the expression control sequence (e.g., promoter) in such a way that facilitates transcription and translation of the coding sequence. As described above, the phrase "genome" indicates that the genome of the cell has been modified. In this case, the recombinant a differentially-regulated gene has been stably integrated into the genome of the animal. The a differentially-regulated gene nucleic acid in operable linkage with the expression control sequence can also be referred to as a construct or transgene.

Any expression control sequence can be used depending on the purpose. For instance, if selective expression is desired, then expression control sequences which limit its expression can be selected. These include, e.g., tissue or cell-specific promoters, introns, enhancers, etc. For various methods of cell and tissue-specific expression, see, e.g., U.S. Pat.

Nos. 6,215,040, 6,210,736, and 6,153,427. These also include the endogenous promoter, i.e., the coding sequence can be operably linked to its own promoter. Inducible and regulatable promoters can also be utilized.

The present invention also relates to a transgenic animal which contains a functionally disrupted and a transgene stably integrated into the animals genome. Such an animal can be constructed using combinations any of the above- and below-mentioned methods. Such animals have any of the aforementioned uses, including permitting the knock-out of the normal gene and its replacement with a mutated gene. Such a transgene can be integrated at the endogenous gene locus so that the functional disruption and "knock-in" are carried out in the same step.

In addition to the methods mentioned above, transgenic animals can be prepared according to known methods, including, e.g., by pronuclear injection of recombinant genes into pronuclei of 1-cell embryos, incorporating an artificial yeast chromosome into

embryonic stem cells, gene targeting methods, embryonic stem cell methodology, cloning methods, nuclear transfer methods. See, also, e.g., U.S. Patent Nos. 4,736,866; 4,873,191; 4,873,316; 5,082,779; 5,304,489; 5,174,986; 5,175,384; 5,175,385; 5,221,778; Gordon et al., Proc. Natl. Acad. Sci., 77:7380-7384, 1980; Palmiter et al., Cell, 41:343-345, 1985; Palmiter et al., Ann. Rev. Genet., 20:465-499, 1986; Askew et al., Mol. Cell. Bio., 13:4115-4124, 1993; Games et al. Nature, 373:523-527, 1995; Valancius and Smithies, Mol. Cell. Bio., 11:1402-1408, 1991; Stacey et al., Mol. Cell. Bio., 14:1009-1016, 1994; Hasty et al., Nature, 350:243-246, 1995; Rubinstein et al., Nucl. Acid Res., 21:2613-2617, 1993; Cibelli et al., Science, 280:1256-1258, 1998. For guidance on recombinase excision systems, see, e.g., U.S. Pat. Nos. 5,626,159, 5,577,695, and 5,434,066. See also, Orban, P. C., et al., "Tissue-Specific DNA Recombination in Transgenic Mice," Proc. Natl. Acad. Sci. USA, 89:6861-6865 (1992); O'Gorman, S., et al., "Recombinase-Mediated Gene Activation and Site-Specific Integration in Mammalian Cells," Science, 251:1351-1355 (1991); Sauer, B., et al., "Cre-stimulated recombination at loxP-Containing DNA sequences placed into the mammalian genome," Polynucleotides Research, 17(1):147-161 (1989); Gagneten, S. et al. (1997) Nucl. Acids Res. 25:3326-3331; Xiao and Weaver (1997) Nucl. Acids Res. 25:2985-2991; Agah, R. et al. (1997) J. Clin. Invest. 100:169-179; Barlow, C. et al. (1997) Nucl. Acids Res. 25:2543-2545; Araki, K. et al. (1997) Nucl. Acids Res. 25:868-872; Mortensen, R. N. et al. (1992) Mol. Cell. Biol. 12:2391-2395 (G418 escalation method); Lakhani, P. P. et al. (1997) Proc. Natl. Acad. Sci. USA 94:9950-9955 ("hit and run"); Westphal and Leder

(1997) Curr. Biol. 7:530-533 (transposon-generated "knock-out" and "knock-in"); Templeton, N. S. et al. (1997) Gene Ther. 4:700-709 (methods for efficient gene targeting, allowing for a high frequency of homologous recombination events, e.g., without selectable markers); PCT International Publication WO 93/22443 (functionally-disrupted).

A polynucleotide according to the present invention can be introduced into any non-human animal, including a non-human mammal, mouse (Hogan et al., Manipulating the Mouse Embryo: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1986), pig (Hammer et al., Nature, 315:343-345, 1985), sheep (Hammer et al., Nature, 315:343-345, 1985), cattle, rat, or primate. See also, e.g., Church, 1987, Trends in Biotech. 5:13-19; Clark et al., Trends in Biotech. 5:20-24, 1987), and DePamphilis et al., BioTechniques, 6:662-680, 1988. Transgenic animals can be produced by the methods described in U.S. Pat. No. 5,994,618, and utilized for any of the utilities described therein.

#### Database

The present invention also relates to electronic forms of polynucleotides, polypeptides, etc., of the present invention, including computer-readable medium (e.g., magnetic, optical, etc., stored in any suitable format, such as flat files or hierarchical files) which comprise such sequences, or fragments thereof, e-commerce-related means, etc. Along these lines, the present invention relates to methods of retrieving gene sequences from a computer-readable medium, comprising, one or more of the following steps in any effective order, e.g., selecting a cell or gene expression profile, e.g., a profile that specifies that said gene is differentially expressed in prostate cancer, and retrieving said differentially expressed gene sequences, where the gene sequences consist of the genes represented by Tables 1 and 2.

A "gene expression profile" means the list of tissues, cells, etc., in which a defined gene is expressed (i.e., transcribed and/or translated). A "cell expression profile" means the genes which are expressed in the particular cell type. The profile can be a list of the tissues in which the gene is expressed, but can include additional information as well, including level of expression (e.g., a quantity as compared or normalized to a control gene), and information on temporal (e.g., at what point in the cell-cycle or developmental program) and spatial expression. By the phrase "selecting a gene or cell expression profile," it is meant that a user decides what type of gene or cell expression pattern he is interested in retrieving, e.g., he may require that the gene is differentially expressed in a tissue, or he may require that the

gene is not expressed in blood, but must be expressed in prostate cancer. Any pattern of expression preferences may be selected. The selecting can be performed by any effective method. In general, "selecting" refers to the process in which a user forms a query that is used to search a database of gene expression profiles. The step of retrieving involves searching for results in a database that correspond to the query set forth in the selecting step. Any suitable algorithm can be utilized to perform the search query, including algorithms that look for matches, or that perform optimization between query and data. The database is information that has been stored in an appropriate storage medium, having a suitable computer-readable format. Once results are retrieved, they can be displayed in any suitable format, such as HTML.

For instance, the user may be interested in identifying genes that are differentially expressed in a prostate cancer. He may not care whether small amounts of expression occur in other tissues, as long as such genes are not expressed in peripheral blood lymphocytes. A query is formed by the user to retrieve the set of genes from the database having the desired gene or cell expression profile. Once the query is inputted into the system, a search algorithm is used to interrogate the database, and retrieve results.

#### Advertising, licensing, etc., methods

The present invention also relates to methods of advertising, licensing, selling, purchasing, brokering, etc., genes, polynucleotides, specific-binding partners, antibodies, etc., of the present invention. Methods can comprises, e.g., displaying a differentially-regulated gene, a differentially-regulated gene polypeptide, or antibody specific for a differentially-regulated gene in a printed or computer-readable medium (e.g., on the Web or Internet), accepting an offer to purchase said gene, polypeptide, or antibody.

#### Other

A polynucleotide, probe, polypeptide, antibody, specific-binding partner, etc., according to the present invention can be isolated. The term "isolated" means that the material is in a form in which it is not found in its original environment or in nature, e.g., more concentrated, more purified, separated from component, etc. An isolated polynucleotide includes, e.g., a polynucleotide having the sequenced separated from the chromosomal DNA found in a living animal, e.g., as the complete gene, a transcript, or a cDNA. This polynucleotide can be part of a vector or inserted into a chromosome (by

specific gene-targeting or by random integration at a position other than its normal position) and still be isolated in that it is not in a form that is found in its natural environment. A polynucleotide, polypeptide, etc., of the present invention can also be substantially purified. By substantially purified, it is meant that polynucleotide or polypeptide is separated and is essentially free from other polynucleotides or polypeptides, i.e., the polynucleotide or polypeptide is the primary and active constituent. A polynucleotide can also be a recombinant molecule. By "recombinant," it is meant that the polynucleotide is an arrangement or form which does not occur in nature. For instance, a recombinant molecule comprising a promoter sequence would not encompass the naturally-occurring gene, but would include the promoter operably linked to a coding sequence not associated with it in nature, e.g., a reporter gene, or a truncation of the normal coding sequence.

The term "marker" is used herein to indicate a means for detecting or labeling a target. A marker can be a polynucleotide (usually referred to as a "probe"), polypeptide (e.g., an antibody conjugated to a detectable label), PNA, or any effective material.

The topic headings set forth above are meant as guidance where certain information can be found in the application, but are not intended to be the only source in the application where information on such topic can be found.

#### Reference materials

For other aspects of the polynucleotides, reference is made to standard textbooks of molecular biology. See, e.g., Hames et al., Polynucleotide Hybridization, IL Press, 1985; Davis et al., Basic Methods in Molecular Biology, Elsevier Sciences Publishing, Inc., New York, 1986; Sambrook et al., Molecular Cloning, CSH Press, 1989; Howe, Gene Cloning and Manipulation, Cambridge University Press, 1995; Ausubel et al., Current Protocols in Molecular Biology, John Wiley & Sons, Inc., 1994-1998.

The preceding description, utilize the present invention to its fullest extent. The preceding preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limiting the remainder of the disclosure in any way whatsoever. The entire disclosure of all applications, patents and publications, cited above and in the figures are hereby incorporated by reference in their entirety.

## Claims:

1. A method for diagnosing a prostate cancer in a sample comprising prostate tissue, comprising:  
determining the number of target genes which are differentially-regulated in said sample, wherein said target genes are selected from SEQ ID NO 1-211 of claim 26, whereby said number is indicative of the probability that said sample comprises prostate cancer.

2. A method of claim 1, wherein said determining is performed by Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization using polynucleotide probes specific for genes selected from SEQ ID NO 1-211 of claim 26.

3. A method of claim 1, wherein said determining is performed by:  
contacting said sample with a polynucleotide probe under conditions effective for said probe to hybridize specifically to a target nucleic acid in said sample, and detecting the amount of hybridization between said probe and target nucleic acid, and

comparing the amount of hybridization in said sample with the amount of hybridization of said probe in a second sample comprising normal prostate tissue.

4. A method of claim 1, wherein said determining is performed by:  
contacting said sample with a polynucleotide probe under conditions effective for said probe to hybridize specifically to a target nucleic acid in said sample, and detecting the amount of hybridization between said probe and target nucleic acid, and

comparing the amount of hybridization in said sample with the amount of hybridization between a second probe and its corresponding second target nucleic acid in said sample.

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5. A method of claim 2, wherein said probe is a contiguous sequence of at least 8 nucleotides selected from a polynucleotide sequence selected from SEQ ID NOS 1-107 of claim 26, or a complement thereof.

6. A method of assessing a therapeutic or preventative intervention in a subject having a prostate cancer, comprising,  
determining the expression levels in a sample comprising prostate tissue of target genes which are differentially-regulated in prostate cancer, wherein said target genes are selected from SEQ ID NO 1-211 of claim 26.

7. A method of claim 6, wherein the expression levels of at least 10 genes are determined.

8. A method of claim 6, wherein the determining is performed by Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization using polynucleotide probes specific for genes selected from SEQ IDS NO 1-211 of claim 26.

9. A method for identifying agents that modulate the expression of target polynucleotides differentially-regulated in prostate cancer cells, comprising,  
contacting a prostate cell population with a test agent under conditions effective for said test agent to modulate the expression of a target polynucleotide in said cell population, and

determining whether said test agent modulates said target polynucleotide expression, wherein said target polynucleotide is selected from SEQ ID NOS 1-107 of claim 26.

10. A method of claim 9, wherein said agent is an antisense polynucleotide to said target polynucleotide sequence and which is effective to inhibit translation of said target polynucleotide.

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11. A method for identifying agents that modulate a biological activity of a polypeptide differentially-regulated in prostate cancer cells, comprising, contacting a polypeptide differentially-regulated in prostate cancer cells with a test agent under conditions effective for said test agent to modulate a biological activity of said polypeptide, and  
 5 determining whether said test agent modulates said biological activity, wherein said polypeptide is selected from SEQ ID NOS 108-211 of claim 26.

12. A method of treating prostate cancer, comprising, administering to a subject in need thereof a therapeutic agent which is effective for regulating expression of at least one sequence selected from SEQ ID NOS 1-211 of claim  
 10 26.

13. A method of claim 12, wherein said agent is an antibody or an antisense  
 15 which is effective to inhibit translation of said gene.

14. A method of diagnosing a prostate cancer comprising:  
 assessing the expression of at least one gene selected from SEQ ID NO 1-211 of  
 claim 26, wherein said gene is differentially-regulated in said cancer.

15. A method of claim 14, wherein assessing is:  
 measuring mRNA expression levels of said or measuring the expression levels of  
 polypeptide coded for by said gene.

16. A method of claim 14, further comprising:  
 comparing said expression to the expression of said polynucleotide in a known  
 normal tissue.

17. A method of claim 14, wherein said assessing detecting is performed by:  
 Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR,  
 RACE PCR, or *in situ* hybridization, and  
 using a polynucleotide probe specific for a polynucleotide sequence selected from  
 5 SEQ ID NOS 1-107 of claim 26.

18. A method of claim 14, wherein the expression of at least one up-regulated  
 polynucleotide and at least one down-regulated polynucleotide are assessed.

19. A method of claim 14, wherein the expression of at least five up-regulated  
 polynucleotides and at least five down-regulated polynucleotides are assessed.

20. A method of retrieving prostate cancer differentially-regulated gene  
 sequences from a computer-readable medium, comprising:  
 15 selecting a gene expression profile that specifies that said gene is differentially-  
 regulated in a prostate cancer, and retrieving prostate cancer differentially-regulated gene  
 sequences,

where the gene sequences consist of genes selected from SEQ ID NO 1-211 of claim  
 26.

21. An ordered array of polynucleotide probes for detecting the expression of  
 differentially-regulated prostate cancer genes in a sample, comprising:  
 polynucleotide probes associated with a solid support, wherein each probe is specific  
 for a different differentially-regulated prostate cancer gene, and the probes are specific for  
 25 genes selected from SEQ ID NO 1-211 of claim 26.

22. An array of claim 21, wherein said array comprises probes specific for up-  
 regulated and down-regulated polynucleotides.

23. A method of advertising for sale, commercial use, or licensing, comprising:  
 displaying at least one polynucleotide or polypeptide sequence selected from

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SEQ ID NO 1-211 of claim 26, or a complement thereto.

24. A non-human, transgenic mammal having a functional disruption in at least one gene selected from SEQ ID NO 1-211 of claim 26, and which is susceptible to prostate cancer.

25. A cell expression profile consisting of the expression pattern of a prostate cancer tissue sample for differentially-regulated genes of claim 26.

26. A plurality of genes which are differentially regulated in a prostate cancer, selected from:

up-regulated genes having SEQ ID NOS 1-75 and 140-211; and down-regulated genes having SEQ ID 76-107 and 108-139.

Table 1

[illegible]

Table 1

43	180	PC080742U	U	4507186	NM_003125.1	Homo sapiens small proline-rich protein 1B (cornifin)
44	181	PC100113U	U	6647292	AF166330.2	AF166330 Homo sapiens stratum corneum chymotryptic enzyme gene
45	182	PC100356U	U	3093334	HSY17172	Homo sapiens mRNA from HIV-associated non-Hodgkin's lymphoma (clone h12-22)
46	183	PC100428U	U	4502980	NM_001861.1	Homo sapiens cytochrome c oxidase subunit IV (COX4)
47	184	PC090230U	U	3252910	AF056322	Homo sapiens SP100-HMG nuclear autoantigen (SP100) mRNA complete cds
48	184	PC090233U	U	4504192	Homo sapiens general transcription factor IIB (GTF2B) mRNA	
49	185	PC101863U	U	35037	HSNFIV	H. sapiens mRNA for nuclear factor IV
50	186	PC090825U	U	7705215	Homo sapiens H-2K binding factor-2 (LOC51580) mRNA	
51	187	PC101430U	U	609453	M69199.1	(HUMG052A) Human G0S2 protein gene, complete cds
52	188	PC091425U	U	4732025	AF118569	Homo sapiens angiotensin I converting enzyme precursor
53	189	PC010434U	U	4505374	NM_002499.1	Homo sapiens neogenin (chicken) homolog 1
54	190	PC010138U	U	7657203	Homo sapiens acidic 82 kDa protein mRNA (HSU15552) mRNA	
55	191	PC010337U	U	6005813	Homo sapiens serine threonine protein kinase (NDR) mRNA	
56	192	PC010336U	U	7662579	Homo sapiens PRO0644 protein (PRO0644) mRNA	
57	193	PC020185U	U	7669502	NM_013995.1	Homo sapiens lysosomal-associated membrane protein 2
58	194	PC020182U	U	4507164	NM_003113.1	Homo sapiens nuclear antigen Sp100 (SP100) mRNA
59	195	PC030247U	U	348706	HUMCACTHBS	Homo sapiens cathepsin B mRNA 3' UTR with a stem-loop structure providing mRNA stability
60	196	PC030471U	U	31356	HSF1B1	Human mRNA for fibronectin (FN precursor)
61	197	PC030454U	U	4506678	Homo sapiens ribosomal protein S10 (RPS10) mRNA	
62	198	PC030326U	U	4507148	Homo sapiens superoxide dismutase 1 soluble (amyotrophic lateral sclerosis 1 (adult)) (SOD1) mRNA	
63	199	PC030425U	U	415818	HSMDQ67	H. sapiens mku67a mRNA (long type) for antigen of monoclonal antibody K6-67
64	200	PC091527U	U	5803091	Homo sapiens methionine aminopeptidase: eIF-2-associated p67 (MNPEP) mRNA	
65	201	PC092004U	U	8922823	NM_018300.1	Homo sapiens hypothetical protein FLJ11015 (FLJ11015)
66	202	PC091888U	U	4757809	Homo sapiens ATP synthase H+ transporting mito F1 complex alpha subunit isoform 1 cardiac muscle (ATP5A1) nuclear gene	
67	203	PC091853U	U	31091	X16869.1	HSF1AC Human mRNA for elongation factor 1-alpha
68	204	PC092052U	U	4505634	Homo sapiens BH-protocadherin (brain-heart) (9999DH7) mRNA	
69	205	PC091839U	U	7188646	AF222043	Homo sapiens ubiquitin-associated protein (NAG20) mRNA complete cds
70	206	PC111181U	U	7416940	AF139077	Homo sapiens MS-14 mRNA complete cds
71	207	PC111168U	U	4759283	NM_004181.1	Homo sapiens ubiquitin carboxyl-terminal esterase L1
72	208	PC120136U	U	7706728	Homo sapiens TBX3-iso protein (TBX3-iso) mRNA	
73	209	PC120331U	U	4504424	NM_002128.1	Homo sapiens high-mobility group (nonhistone chromosomal) protein 1
74	210	PC121671U	U	7861635	Homo sapiens DKFZP564O2082 protein (DKFZP564O2082) mRNA	
75	211	PC020741U	U	7857624	NM_014393.1	Homo sapiens staufen (Drosophila, RNA-binding protein) homolog 2
153	212	PC051231U	U	4506600	Homo sapiens ribosomal protein L14 (RPL14) mRNA	
		PC020627U	U	8923949	Homo sapiens ovarian cancer related protein OVN9-3 (OVN9-3) mRNA	
		PC110927U	U	8923282	NM_017754.1	Homo sapiens hypothetical protein FLJ20302 (FLJ20302)

Table 2

DNA SEQ ID	Prs SEQ ID	Identifier	Exp	Cl#	Gene Name and Description
76	108	PC040734D	D	5174656	NM_006096.1  Homo sapiens differentiation-related gene 1 nickel-specific induction protein
77	109	PC040156D	D	4505748	Homo sapiens phosphofructokinase muscle (PFKM) mRNA
78	110	PC051745D	D	4758751	Homo sapiens neuronal apoptosis inhibitory protein (NAIP) mRNA
79	111	PC042021D	D	4505986	Homo sapiens PTPRF interacting protein binding protein 1 (lipin beta 1) (PPF1BP1) mRNA and translated products
80	112	PC060144D	D	4758199	NM_004415.1  Homo sapiens desmoplakin (DPI, DP10) (DSP) mRNA
81	113	PC080139D	D	7657159	NM_014362.1  Homo sapiens 3-hydroxyisobutyryl-Coenzyme A hydrolase (HIBCH), mRNA
82	114	PC080435D	D	4758807	Homo sapiens ras GTPase activating protein-like (NGAP) mRNA
83	115	PC070436D	D	9790904	NM_001924.1  Homo sapiens growth arrest and DNA-damage-inducible
84	116	PC061342D	D	186483	HUMINT04 Human leukocyte adhesion protein p15095 alpha subunit gene exons 16 - 21
85	117	PC060793D	D	4507582	NM_000043.1  Homo sapiens tumor necrosis factor receptor superfamily
86	118	PC060743D	D	4557256	Homo sapiens adenylate cyclase 8 (brain) (ADCY8) mRNA
87	119	PC061528D	D	4506700	Homo sapiens ribosomal protein S23 (RPS23) mRNA
88	120	PC090788D	D	5031638	Homo sapiens cornichon-like (CNIL) mRNA
89	121	PC090722D	D	7670747	AF227906 Homo sapiens UDP-glucose 6-epimerase glucosyltransferase 2 precursor mRNA complete cds
90	122	PC071770D	D	31441	HSFNRB Human mRNA for integrin beta 1 subunit
91	123	PC090677D	D	187701	HUMMHBA123 Human MHC protein homologous to chicken B complex protein mRNA complete cds
92	124	PC101847D	D	5902021	Homo sapiens PL6 protein (PL6) mRNA
93	125	PC090622D	D	4506858	NM_002997.1  Homo sapiens syndecan 1 (SDC1) mRNA
94	126	PC010433D	D	4827043	Homo sapiens thyroid hormone receptor-associated protein 240 kDa subunit (TRAP240) mRNA
95	127	PC020238D	D	4503090	NM_001893.1  Homo sapiens casein kinase I, delta (CSNK1D) mRNA
96	128	PC030301D	D	4506728	Homo sapiens ribosomal protein S5 (RPS5) mRNA
97	129	PC110249D	D	4759257	Homo sapiens Ac-like transposable element (ALTE) mRNA
98	130	PC110541D	D	5031778	Homo sapiens interferon gamma-inducible protein 16 (IFI16) mRNA
99		PC110431D	D	3885367	AB019564 Homo sapiens mRNA expressed only in placental villi clone SMAP47
100	131	PC110940D	D	4758949	NM_000942.1  Homo sapiens peptidylprolyl isomerase B (cyclophilin B)
101	132	PC111588D	D	4503412	Homo sapiens diphtheria toxin receptor (heparin-binding epidermal growth factor-like growth factor) (DTR) mRNA
102	133	PC111669D	D	7705822	Homo sapiens N-terminal acetyltransferase complex and subunit (LOC51126) mRNA
103	134	PC032046D	D	7657325	NM_014623.1  Homo sapiens male-enhanced antigen (MEA),
104	135	PC120741D	D	5174388	NM_005891.1  Homo sapiens acetyl-Coenzyme A acetyltransferase 2
105	136	PC120740D	D	311180	HSTCP1 Human t-complex polypeptide 1 gene
106	137	PC010853D	D	4506660	Homo sapiens ribosomal protein L7a (RPL7A) mRNA
107	139	PC030968D	D	4507668	Homo sapiens tumor protein translationally-controlled 1 (TPT1) mRNA
138		PC031146D	D	8924228	NM_018636.1  Homo sapiens hypothetical protein PRO2987 (PRO2987)

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Table 3

PC052029U	U	5803219		Kazal	Kazal-type serine protease inhibitor	172.5	3.70E-49	993	1046		
PC052029U	U	5803219		RNA POL M 15K	RNA polymerases M15 Kd subunit	-7.8	6.40E-01	308	363		
PC052029U	U	5803219		DnaJ CXXCXXG	DnaJ central domain (4 repeats)	-51.3	6.50E-01	751	823		
PC052029U	U	5803219		Hindin	Hindin	-10.8	7.40E-01	350	441		
PC093	PC052029U	U	641958	HMGB1	Human nonmuscle myosin heavy chain-B (NM-H2B)	1149.3	0.00E+00	187	211		
PC052029U	U	641958		myosin head	Myosin head (motor domain)	148.7	1.20E-24	1071	1931		
PC052029U	U	641958		myosin tail	Myosin tail	76.1	3.70E-20	1898	1918		
PC052029U	U	641958		M	M protein repeat	70.1	2.40E-18	33	77		
PC052029U	U	641958		Myosin N	Myosin N-terminal SH3-like domain	27.3	5.90E-04	787	807		
PC052029U	U	641958		IQ	IQ chromodulin-binding motif	-98.6	6.60E-02	1083	1318		
PC052029U	U	641958		Apolipoprotein	Apolipoprotein A1/A4/E family	-86.6	8.70E-02	1018	1250		
PC052029U	U	641958		DUF164	Uncharacterized ACR, COG1579	7.2	8.80E-02	1788	1817		
PC052029U	U	641958		bZIP	bZIP transcription factor	-394.9	9.50E-02	171	425		
PC052029U	U	641958		Prismane	Prismane	-35.3	1.20E-01	965	1062		
PC052029U	U	641958		K-box	K-box region	0.1	1.30E-01	742	748		
PC052029U	U	641958		Tub	Tub family	3.2	1.80E-01	1863	1898		
PC052029U	U	641958		Tropomyosin	Tropomyosin	2.7	1.80E-01	1781	1809		
PC052029U	U	641958		Lipoprotein I	Borrelia lipoprotein	-4.6	2.10E-01	1034	1108		
PC052029U	U	641958		HRI	Hri repeat motif	-414.1	2.20E-01	600	996		
PC052029U	U	641958		HSP70	Hsp70 protein	-38.3	2.70E-01	1488	1684		
PC052029U	U	641958		OEP	Outer membrane efflux protein	10.5	3.30E-01	1823	1832		
PC052029U	U	641958		Involucrin	Involucrin repeat	3.1	3.30E-01	1531	1548		
PC052029U	U	641958		kinesin	Kinesin motor domain	-47.4	4.00E-01	1062	1165		
PC052029U	U	641958		KE2	KE2 family protein	-65	5.30E-01	863	1220		
PC052029U	U	641958		HlyD	HlyD family secretion protein	2.5	5.40E-01	1107	1127		
PC052029U	U	641958		NAP family	Nucleosome assembly protein (NAP)	-4.5	6.10E-01	1043	1077		
PC052029U	U	641958		UVR	UvrB/UvrC motif	-36.2	7.30E-01	1232	1353		
PC052029U	U	641958		Birna VP5	Birnavirus VP5 protein	-110.7	7.90E-01	1325	1534		
PC052029U	U	641958		BAR	BAR domain	1	8.20E-01	1304	1317		
PC052029U	U	641958		Transaldolase	Transaldolase	10.5	9.60E-01	1182	1210		
PC129	PC060144D	D	4758200	Down-regulated	NM004415.1 (Homo sapiens) cDNA clone (DPI/DP1/DP2/DP3/DP4/DP5/DP6/DP7/DP8/DP9/DP10/DP11/DP12/DP13/DP14/DP15/DP16/DP17/DP18/DP19/DP20/DP21/DP22/DP23/DP24/DP25/DP26/DP27/DP28/DP29/DP30/DP31/DP32/DP33/DP34/DP35/DP36/DP37/DP38/DP39/DP40/DP41/DP42/DP43/DP44/DP45/DP46/DP47/DP48/DP49/DP50/DP51/DP52/DP53/DP54/DP55/DP56/DP57/DP58/DP59/DP60/DP61/DP62/DP63/DP64/DP65/DP66/DP67/DP68/DP69/DP70/DP71/DP72/DP73/DP74/DP75/DP76/DP77/DP78/DP79/DP80/DP81/DP82/DP83/DP84/DP85/DP86/DP87/DP88/DP89/DP90/DP91/DP92/DP93/DP94/DP95/DP96/DP97/DP98/DP99/DP100/DP101/DP102/DP103/DP104/DP105/DP106/DP107/DP108/DP109/DP110/DP111/DP112/DP113/DP114/DP115/DP116/DP117/DP118/DP119/DP120/DP121/DP122/DP123/DP124/DP125/DP126/DP127/DP128/DP129/DP130/DP131/DP132/DP133/DP134/DP135/DP136/DP137/DP138/DP139/DP140/DP141/DP142/DP143/DP144/DP145/DP146/DP147/DP148/DP149/DP150/DP151/DP152/DP153/DP154/DP155/DP156/DP157/DP158/DP159/DP160/DP161/DP162/DP163/DP164/DP165/DP166/DP167/DP168/DP169/DP170/DP171/DP172/DP173/DP174/DP175/DP176/DP177/DP178/DP179/DP180/DP181/DP182/DP183/DP184/DP185/DP186/DP187/DP188/DP189/DP190/DP191/DP192/DP193/DP194/DP195/DP196/DP197/DP198/DP199/DP200/DP201/DP202/DP203/DP204/DP205/DP206/DP207/DP208/DP209/DP210/DP211/DP212/DP213/DP214/DP215/DP216/DP217/DP218/DP219/DP220/DP221/DP222/DP223/DP224/DP225/DP226/DP227/DP228/DP229/DP230/DP231/DP232/DP233/DP234/DP235/DP236/DP237/DP238/DP239/DP240/DP241/DP242/DP243/DP244/DP245/DP246/DP247/DP248/DP249/DP250/DP251/DP252/DP253/DP254/DP255/DP256/DP257/DP258/DP259/DP260/DP261/DP262/DP263/DP264/DP265/DP266/DP267/DP268/DP269/DP270/DP271/DP272/DP273/DP274/DP275/DP276/DP277/DP278/DP279/DP280/DP281/DP282/DP283/DP284/DP285/DP286/DP287/DP288/DP289/DP290/DP291/DP292/DP293/DP294/DP295/DP296/DP297/DP298/DP299/DP300/DP301/DP302/DP303/DP304/DP305/DP306/DP307/DP308/DP309/DP310/DP311/DP312/DP313/DP314/DP315/DP316/DP317/DP318/DP319/DP320/DP321/DP322/DP323/DP324/DP325/DP326/DP327/DP328/DP329/DP330/DP331/DP332/DP333/DP334/DP335/DP336/DP337/DP338/DP339/DP340/DP341/DP342/DP343/DP344/DP345/DP346/DP347/DP348/DP349/DP350/DP351/DP352/DP353/DP354/DP355/DP356/DP357/DP358/DP359/DP360/DP361/DP362/DP363/DP364/DP365/DP366/DP367/DP368/DP369/DP370/DP371/DP372/DP373/DP374/DP375/DP376/DP377/DP378/DP379/DP380/DP381/DP382/DP383/DP384/DP385/DP386/DP387/DP388/DP389/DP390/DP391/DP392/DP393/DP394/DP395/DP396/DP397/DP398/DP399/DP400/DP401/DP402/DP403/DP404/DP405/DP406/DP407/DP408/DP409/DP410/DP411/DP412/DP413/DP414/DP415/DP416/DP417/DP418/DP419/DP420/DP421/DP422/DP423/DP424/DP425/DP426/DP427/DP428/DP429/DP430/DP431/DP432/DP433/DP434/DP435/DP436/DP437/DP438/DP439/DP440/DP441/DP442/DP443/DP444/DP445/DP446/DP447/DP448/DP449/DP450/DP451/DP452/DP453/DP454/DP455/DP456/DP457/DP458/DP459/DP460/DP461/DP462/DP463/DP464/DP465/DP466/DP467/DP468/DP469/DP470/DP471/DP472/DP473/DP474/DP475/DP476/DP477/DP478/DP479/DP480/DP481/DP482/DP483/DP484/DP485/DP486/DP487/DP488/DP489/DP490/DP491/DP492/DP493/DP494/DP495/DP496/DP497/DP498/DP499/DP500/DP501/DP502/DP503/DP504/DP505/DP506/DP507/DP508/DP509/DP510/DP511/DP512/DP513/DP514/DP515/DP516/DP517/DP518/DP519/DP520/DP521/DP522/DP523/DP524/DP525/DP526/DP527/DP528/DP529/DP530/DP531/DP532/DP533/DP534/DP535/DP536/DP537/DP538/DP539/DP540/DP541/DP542/DP543/DP544/DP545/DP546/DP547/DP548/DP549/DP550/DP551/DP552/DP553/DP554/DP555/DP556/DP557/DP558/DP559/DP560/DP561/DP562/DP563/DP564/DP565/DP566/DP567/DP568/DP569/DP570/DP571/DP572/DP573/DP574/DP575/DP576/DP577/DP578/DP579/DP580/DP581/DP582/DP583/DP584/DP585/DP586/DP587/DP588/DP589/DP590/DP591/DP592/DP593/DP594/DP595/DP596/DP597/DP598/DP599/DP600/DP601/DP602/DP603/DP604/DP605/DP606/DP607/DP608/DP609/DP610/DP611/DP612/DP613/DP614/DP615/DP616/DP617/DP618/DP619/DP620/DP621/DP622/DP623/DP624/DP625/DP626/DP627/DP628/DP629/DP630/DP631/DP632/DP633/DP634/DP635/DP636/DP637/DP638/DP639/DP640/DP641/DP642/DP643/DP644/DP645/DP646/DP647/DP648/DP649/DP650/DP651/DP652/DP653/DP654/DP655/DP656/DP657/DP658/DP659/DP660/DP661/DP662/DP663/DP664/DP665/DP666/DP667/DP668/DP669/DP670/DP671/DP672/DP673/DP674/DP675/DP676/DP677/DP678/DP679/DP680/DP681/DP682/DP683/DP684/DP685/DP686/DP687/DP688/DP689/DP690/DP691/DP692/DP693/DP694/DP695/DP696/DP697/DP698/DP699/DP700/DP701/DP702/DP703/DP704/DP705/DP706/DP707/DP708/DP709/DP710/DP711/DP712/DP713/DP714/DP715/DP716/DP717/DP718/DP719/DP720/DP721/DP722/DP723/DP724/DP725/DP726/DP727/DP728/DP729/DP730/DP731/DP732/DP733/DP734/DP735/DP736/DP737/DP738/DP739/DP740/DP741/DP742/DP743/DP744/DP745/DP746/DP747/DP748/DP749/DP750/DP751/DP752/DP753/DP754/DP755/DP756/DP757/DP758/DP759/DP760/DP761/DP762/DP763/DP764/DP765/DP766/DP767/DP768/DP769/DP770/DP771/DP772/DP773/DP774/DP775/DP776/DP777/DP778/DP779/DP780/DP781/DP782/DP783/DP784/DP785/DP786/DP787/DP788/DP789/DP790/DP791/DP792/DP793/DP794/DP795/DP796/DP797/DP798/DP799/DP800/DP801/DP802/DP803/DP804/DP805/DP806/DP807/DP808/DP809/DP810/DP811/DP812/DP813/DP814/DP815/DP816/DP817/DP818/DP819/DP820/DP821/DP822/DP823/DP824/DP825/DP826/DP827/DP828/DP829/DP830/DP831/DP832/DP833/DP834/DP835/DP836/DP837/DP838/DP839/DP840/DP841/DP842/DP843/DP844/DP845/DP846/DP847/DP848/DP849/DP850/DP8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 <211> 619  
 <212> DNA  
 <213> Homo sapiens

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 gccctgcac ccaaggtgc ctgagcctg ccaaccnaa gtgctgagc ctgctagcc 240  
 caagcttca ggcctatgc acccaagt gtctgagccc tgcctttcaa tagtaactc 300  
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 agcggccac cagatgtgta atccctalc ccaatctgt tatgagccc atttgctgt 420  
 caattagcat ttgtctccc ccaaaaaga atgtgctat agcttttct ttctacac 480  
 tctgagctc tgaatgagc tgaagttct agtaccagc ctagttttca gctgtcaga 540  
 attcatctga agagagact aagatgaag caatgaltt agtctctta taccctatt 600  
 aaattcaatt tcaattcca 619

<210> 44  
 <211> 762  
 <212> DNA  
 <213> Homo sapiens

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 atgagcgtt ggtgtctac tgcgcccac tgaagatga atgagtacac ctgtcactg 240  
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 tctgactca tptgtgga tgcagctc atctccccc agpacagac gaagtttcc 540  
 aagacttac tgaatatic catgtgtg gctggctcc cgaactcna gaaaacgpc 600  
 tgaatgtg actcagggg accgtgtg tgcagagta cctgcagag tctgtatcc 660  
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<210> 45  
 <211> 322  
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 <213> Homo sapiens

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 ccaaaaatg ctatgtcat actcttcaat cagccacata gccctgtag taacagcat 180  
 tctatcnaa accctctgaa gctcagcg cgcagctatt ctctaatcg cccagagct 240  
 tactatcca ttactattt gctagcact ctacagctc tencagacc gccacataa 300  
 agatgcgcc cactccaaa aa 322

<210> 46  
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 <212> DNA  
 <213> Homo sapiens

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 gacacgggtt gtagagggcg gtcgcgcgc gcaatggcg cagatgtgt gctacaggg 180  
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 agtgaagaa gtagagatg ctggctctg cctgcactg cgcctgctc tgcaccgcu 720  
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<210> 47  
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 <212> DNA  
 <213> Homo sapiens

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 gacatttca ttctctgag gctctcgta tegtgtctc atccaaata aaatgttga 300  
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 gtacttta cctaaaggt gtcagata agtaactaa agaaagaga agtttctg 3480  
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 <212> DNA  
 <213> Homo sapiens

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 accatcag caccatcac cctcttacc ctctactct acctagcct aactactcc 180  
 acctcaaa cactactcc catatctac aagtaaaaa taatatgaa gtttaacaa 240  
 caaaacccc ccaattccc ccaacatca tgcctctac cagctactc ctactatct 300  
 cccctttat actaatag tctgttgtt ctgttgcg gaccgcagt cgcctgag 360  
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<211> 2969  
<212> DNA  
<213> Homo sapiens

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<212> DNA  
<213> Homo sapiens

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 Gly Thr Val Ile Gly Ser Ala Arg Cys Lys Asp Phe Arg Glu Arg Glu  
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 Gly Arg Leu Arg Ala Ala Tyr Asn Leu Val Lys Arg Gly Ile Thr Asn  
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 Arg Ser Glu Trp Ser Asp Leu Leu Ser Asp Leu Gln Lys Ala Gly Lys  
 130 135 140  
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Asn Val Leu Gly His Met Gln Gln Gly Gly Ser Pro Thr Pro Phe Asp 670  
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 Cys Ile Leu Arg Lys Leu Phe Ser His Asn Met Thr Arg Leu Arg Lys  
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Phe Met Val Tyr Phe Gly Lys Asn Gln Ser Leu Gln Lys Ile Gln Lys  
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Arg Asp Leu Gly Glu Ser Asn Ser Asp Leu Asp Met Pro Phe Ala Lys 635  
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Trp Leu Asp Ile Gly Leu Pro Glu Tyr Lys Thr Glu Phe Asp Glu 735  
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Gly Arg Val Asp Gly Arg Met Leu His Tyr Met Thr Val Asp Asp Leu 740 750  
Leu Ser Leu Lys Val Val Ser Val Leu His His Leu Ser Ile Lys Arg 755 765  
Ala Ile Gln Val Leu Arg Ile Asn Asn Phe Glu Pro Asn Cys Leu Arg 770 780  
Arg Arg Pro Ser Asp Glu Asn Thr Ile Ala Pro Ser Glu Val Gln Lys 785 795  
Trp Thr Asn His Arg Val Met Glu Trp Leu Arg Ser Val Asp Leu Ala 800 815  
Glu Tyr Ala Pro Asn Leu Arg Gly Ser Gly Val His Gly Gly Leu Met 820 830  
Val Leu Glu Pro Arg Phe Asn Val Glu Thr Met Ala Gln Leu Leu Asn 835 845  
Ile Pro Pro Asn Lys Thr Leu Leu Arg Arg His Leu Ala Thr His Phe 850 860  
Asn Leu Leu Ile Gly Ala Glu Ala Gln His Gln Lys Arg Ala Met 865 875  
Glu Leu Pro Asp Tyr Val Leu Leu Thr Ala Thr Ala Lys Val Lys Pro 880 895  
Lys Lys Leu Ala Phe Ser Asn Phe Gly Asn Leu Arg Lys Lys Gln 900 910  
Glu Asp Gly Glu Glu Tyr Val Cys Pro Met Glu Leu Cys Gln Ala Ser 915 925  
Gly Ser Ala Ser Lys Lys Gly Phe Lys Pro Gly Leu Asp Met Arg Leu 930 940  
Tyr Glu Glu Asp Asp Leu Asp Arg Leu Glu Gln Met Glu Asp Ser Glu 945 955  
Gly Thr Val Arg Gln Ile Gly Ala Phe Ser Glu Gly Ile Asn Asn Leu 960 975  
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Thr Asp Gln Asn Ser Asp Gly Tyr Cys Gln Thr Gly Thr Met Ser Arg 50 55 60  
His Gln Asn Gln Asn Thr Ile Gln Glu Leu Leu Gln Asn Cys Ser Asp 65 70 75  
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Gln Ala Asn Asp Gln Met Glu Ile Leu Asp Ser Leu Ile Arg Glu Met 115 120 125  
Arg Gln Met Gly Gln Pro Cys Asp Ala Tyr Gln Lys Arg Leu Leu Gln 130 135 140  
Leu Gln Glu Gln Met Arg Ala Leu Tyr Lys Ala Ile Ser Val Pro Arg 145 150 155 160  
Val Arg Arg Ala Ser Ser Lys Gly Gly Gly Tyr Thr Cys Gln Ser 165 170 175  
Gly Ser Gly Trp Asp Glu Phe Thr Lys His Val Thr Ser Glu Cys Leu 180 185 190  
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His Asn Ser Ile Gly Asp Tyr Arg Trp Gln Leu Asp Lys Ile Lys Ala 225 230 235 240  
Asp Leu Arg Glu Lys Ser Ala Ile Tyr Gln Leu Glu Glu Tyr Glu 245 250 255  
Asn Leu Leu Lys Ala Ser Phe Glu Arg Met Asp His Leu Arg Gln Leu 260 265 270  
Gln Asn Ile Ile Gln Ala Thr Ser Arg Glu Ile Met Trp Ile Asn Asp 275 280 285  
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Val Lys Glu Lys Glu Leu Asn Lys Leu Lys Gln Glu Ser Asp Gln Leu 325 330 335

Val Leu Asn Gln His Pro Ala Ser Asp Lys Ile Glu Ala Tyr Met Asp  
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Thr Leu Gln Thr Gln Trp Ser Trp Ile Leu Gln Ile Thr Lys Cys Ile  
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Asp Val His Leu Lys Glu Asn Ala Ala Tyr Phe Gln Phe Glu Glu  
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Ala Gln Ser Thr Glu Ala Tyr Leu Lys Gly Leu Gln Asp Ser Ile Arg  
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Lys Lys Tyr Pro Cys Asp Lys Asn Met Pro Leu Gln His Leu Leu Glu  
405 410 415

Gln Ile Lys Glu Leu Glu Lys Glu Arg Glu Lys Ile Leu Glu Tyr Lys  
420 425 430

Arg Gln Val Gln Asn Leu Val Asn Lys Ser Lys Lys Ile Val Gln Leu  
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Lys Pro Arg Asn Pro Asp Tyr Arg Ser Asn Lys Pro Ile Ile Leu Arg  
450 455 460

Ala Leu Cys Asp Tyr Lys Gln Asp Gln Lys Ile Val His Lys Gly Asp  
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Glu Cys Ile Leu Lys Asp Asn Asn Glu Arg Ser Lys Trp Tyr Val Thr  
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Gly Pro Gly Gly Val Asp Met Leu Val Pro Ser Val Gly Leu Ile Ile  
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Pro Pro Pro Asn Pro Leu Ala Val Asp Leu Ser Cys Lys Ile Glu Gln  
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Lys Ser Leu Val Ser Trp His Tyr Cys Met Ile Asp Ile Glu Lys Ile  
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Arg Ala Met Thr Ile Ala Lys Leu Lys Thr Met Arg Gln Glu Asp Tyr  
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Met Lys Thr Ile Ala Asp Leu Glu Leu His Tyr Gln Glu Phe Ile Arg  
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Asn Ser Gln Gly Ser Glu Met Phe Gly Asp Asp Lys Arg Lys Ile  
595 600 605

Gln Ser Gln Phe Thr Asp Ala Gln Lys His Tyr Gln Thr Leu Val Ile  
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Gln Leu Pro Gly Tyr Pro Gln His Gln Thr Val Thr Thr Glu Ile  
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Thr His His Gly Thr Cys Gln Asp Val Asn His Asn Lys Val Ile Glu

645 650 655

Thr Asn Arg Glu Asn Asp Lys Gln Glu Thr Trp Met Leu Met Glu Leu  
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Gln Lys Ile Arg Arg Gln Ile Glu His Cys Glu Gly Arg Met Thr Leu  
675 680 685

Lys Asn Leu Pro Leu Ala Asp Gln Gly Ser Ser His His Ile Thr Val  
690 695 700

Lys Ile Asn Glu Leu Lys Ser Val Gln Asn Asp Ser Gln Ala Ile Ala  
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Glu Val Leu Asn Gln Leu Lys Asp Met Leu Ala Asn Phe Arg Gly Ser  
725 730 735

Glu Lys Tyr Cys Tyr Leu Gln Asn Glu Val Phe Gly Leu Phe Gln Lys  
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770 775 780

Lys Val Tyr Glu Ala Arg Leu Thr Glu Glu Glu Thr Val Cys Leu Asp  
785 790 795 800

Leu Asp Lys Val Glu Ala Tyr Arg Cys Gly Leu Lys Lys Ile Lys Asn  
805 810 815

Asp Leu Asn Leu Lys Lys Ser Leu Leu Ala Thr Met Lys Thr Glu Leu  
820 825 830

Gln Lys Ala Gln Gln Ile His Ser Gln Thr Ser Gln Gln Tyr Pro Leu  
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850 855 860

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885 890 895

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Lys Asn Lys Phe Leu Asp Gln Asn Leu Gln Lys Tyr Gln Ala Glu 1055  
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Cys Ser Gln Phe Lys Ala Lys Leu Ala Ser Leu Glu Glu Leu Lys 1070  
1075  
Arg Gln Ala Glu Leu Asp Gly Lys Ser Ala Lys Gln Asn Leu Asp 1085  
1090  
Lys Cys Tyr Gly Gln Ile Lys Glu Leu Asn Glu Lys Ile Thr Arg 1100  
1105  
Leu Thr Tyr Glu Ile Glu Asp Glu Lys Arg Arg Lys Ser Val 1115  
1120  
Glu Asp Arg Phe Asp Gln Gln Lys Asn Asp Tyr Asp Gln Leu Gln 1130  
1135  
Lys Ala Arg Gln Cys Glu Lys Glu Asn Leu Gly Trp Gln Lys Leu 1145  
1150  
Glu Ser Glu Lys Ala Ile Lys Glu Lys Glu Tyr Glu Ile Glu Arg 1160  
1165  
Leu Arg Val Leu Leu Gln Glu Glu Gly Thr Arg Lys Arg Glu Tyr 1175  
1180  
Glu Asn Glu Leu Ala Lys Val Arg Asn His Tyr Asn Glu Glu Met 1190  
1195  
Ser Asn Leu Arg Asn Lys Tyr Glu Thr Glu Ile Asn Ile Thr Lys 1205  
1210  
Thr Thr Ile Lys Glu Ile Ser Met Gln Lys Glu Asp Asp Ser Lys 1220  
1225  
Asn Leu Arg Asn Gln Leu Asp Arg Leu Ser Arg Glu Asn Arg Asp 1235  
1240  
Leu Lys Asp Glu Ile Val Arg Leu Asn Asp Ser Ile Leu Gln Ala 1250  
1255

Thr Glu Gln Arg Arg Arg Ala Glu Glu Asn Ala Leu Gln Gln Lys 1265  
1270  
Ala Cys Gly Ser Glu Ile Met Gln Lys Lys Gln His Leu Glu Ile 1280  
1285  
Glu Leu Lys Gln Val Met Gln Gln Arg Ser Glu Asp Asn Ala Arg 1295  
1300  
His Lys Gln Ser Leu Glu Glu Ala Ala Lys Thr Ile Gln Asp Lys 1310  
1315  
Asn Lys Glu Ile Glu Arg Leu Lys Ala Glu Phe Gln Glu Glu Ala 1325  
1330  
Lys Arg Arg Trp Glu Tyr Glu Asn Glu Leu Ser Lys Val Arg Asn 1340  
1345  
Asn Tyr Asp Glu Glu Ile Ile Ser Leu Lys Asn Gln Phe Glu Thr 1355  
1360  
Glu Ile Asn Ile Thr Lys Thr Thr Ile His Gln Leu Thr Met Gln 1370  
1375  
Lys Glu Glu Asp Thr Ser Gly Tyr Arg Ala Gln Ile Asp Asn Leu 1385  
1390  
Thr Arg Glu Asn Arg Ser Leu Ser Glu Glu Ile Lys Arg Leu Lys 1400  
1405  
Asn Thr Leu Thr Gln Thr Thr Glu Asn Leu Arg Arg Val Glu Glu 1415  
1420  
Asp Ile Gln Gln Gln Lys Ala Thr Gly Ser Glu Val Ser Gln Arg 1430  
1435  
Lys Gln Gln Leu Glu Val Glu Leu Arg Gln Val Thr Gln Met Arg 1445  
1450  
Thr Glu Glu Ser Val Arg Tyr Lys Gln Ser Leu Asp Asp Ala Ala 1460  
1465  
Lys Thr Ile Gln Asp Lys Asn Lys Glu Ile Glu Arg Leu Lys Gln 1475  
1480  
Leu Ile Asp Lys Glu Thr Asn Asp Arg Lys Cys Leu Glu Asp Glu 1490  
1495  
Asn Ala Arg Leu Gln Arg Val Gln Tyr Asp Leu Gln Lys Ala Asn 1505  
1510  
Ser Ser Ala Thr Glu Thr Ile Asn Lys Leu Lys Val Gln Glu Gln 1520  
1525  
Glu Leu Thr Arg Leu Arg Ile Asp Tyr Glu Arg Val Ser Gln Glu 1535  
1540  
Arg Thr Val Lys Asp Gln Asp Ile Thr Arg Phe Gln Asn Ser Leu 1550  
1555

Lys Glu Leu Gln Gln Lys Gln Lys Val Glu Glu Glu Leu Asn  
1565 1570 1575

Arg Leu Lys Arg Thr Ala Ser Glu Asp Ser Cys Lys Arg Lys Lys  
1580 1585 1590 1595

Leu Glu Glu Glu Leu Glu Gly Met Arg Arg Ser Leu Lys Glu Gln  
1595 1600 1605

Ala Ile Lys Ile Thr Asn Leu Thr Gln Gln Leu Glu Gln Ala Ser  
1610 1615 1620

Ile Val Lys Lys Arg Ser Glu Asp Asp Leu Arg Gln Gln Arg Asp  
1625 1630 1635

Val Leu Asp Gly His Leu Arg Glu Lys Gln Arg Thr Gln Glu Glu  
1640 1645 1650

Leu Arg Arg Leu Ser Ser Glu Val Glu Ala Leu Arg Arg Gln Leu  
1655 1660 1665

Leu Gln Glu Gln Glu Ser Val Lys Gln Ala His Leu Arg Asn Glu  
1670 1675 1680

His Phe Gln Lys Ala Ile Glu Asp Lys Ser Arg Ser Leu Asn Glu  
1685 1690 1695

Ser Lys Ile Glu Ile Glu Arg Leu Gln Ser Leu Thr Glu Asn Leu  
1700 1705 1710

Thr Lys Glu His Leu Met Leu Glu Glu Leu Arg Asn Leu Arg  
1715 1720 1725

Leu Glu Tyr Asp Asp Leu Arg Arg Gly Arg Ser Glu Ala Asp Ser  
1730 1735 1740

Asp Lys Asn Ala Thr Ile Leu Glu Leu Arg Ser Gln Leu Gln Ile  
1745 1750 1755

Ser Asn Asn Arg Thr Leu Glu Leu Gln Gly Leu Ile Asn Asp Leu  
1760 1765 1770

Gln Arg Glu Arg Glu Asn Leu Arg Gln Glu Ile Glu Lys Phe Gln  
1775 1780 1785

Lys Gln Ala Leu Glu Ala Ser Asn Arg Ile Gln Glu Ser Lys Asn  
1790 1795 1800

Gln Cys Thr Gln Val Val Gln Glu Arg Glu Ser Leu Leu Val Lys  
1805 1810 1815

Ile Lys Val Leu Glu Gln Asp Lys Ala Arg Leu Gln Arg Leu Glu  
1820 1825 1830

Asp Glu Leu Asn Arg Ala Lys Ser Thr Leu Glu Ala Glu Thr Arg  
1835 1840 1845

Val Lys Gln Arg Leu Glu Cys Glu Lys Gln Gln Ile Gln Asn Asp

1850 1855 1860

Leu Asn Gln Trp Lys Thr Gln Tyr Ser Arg Lys Glu Glu Ala Ile  
1865 1870 1875

Arg Lys Ile Glu Ser Glu Arg Glu Lys Ser Glu Arg Glu Lys Asn  
1880 1885 1890

Ser Leu Arg Ser Glu Ile Glu Arg Leu Gln Ala Glu Ile Lys Arg  
1895 1900 1905

Ile Glu Glu Arg Cys Arg Arg Lys Leu Glu Asp Ser Thr Arg Glu  
1910 1915 1920

Thr Gln Ser Gln Leu Glu Thr Glu Arg Ser Arg Tyr Gln Arg Glu  
1925 1930 1935

Ile Asp Lys Leu Arg Gln Arg Pro Tyr Gly Ser His Arg Glu Thr  
1940 1945 1950

Gln Thr Glu Cys Glu Trp Thr Val Asp Thr Ser Lys Leu Val Phe  
1955 1960 1965

Asp Gly Leu Arg Lys Lys Val Thr Ala Met Gln Leu Tyr Glu Cys  
1970 1975 1980

Gln Leu Ile Asp Lys Thr Thr Leu Asp Lys Leu Leu Lys Gly Lys  
1985 1990 1995

Lys Ser Val Glu Glu Val Ala Ser Glu Ile Gln Pro Phe Leu Arg  
2000 2005 2010

Gly Ala Gly Ser Ile Ala Gly Ala Ser Ala Ser Pro Lys Glu Lys  
2015 2020 2025

Tyr Ser Leu Val Glu Ala Lys Arg Lys Lys Leu Ile Ser Pro Glu  
2030 2035 2040

Ser Thr Val Met Leu Leu Glu Ala Gln Ala Ala Thr Gly Gly Ile  
2045 2050 2055

Ile Asp Pro His Arg Asn Glu Lys Leu Thr Val Asp Ser Ala Ile  
2060 2065 2070

Ala Arg Asp Leu Ile Asp Phe Asp Asp Arg Gln Gln Ile Tyr Ala  
2075 2080 2085

Ala Glu Lys Ala Ile Thr Gly Phe Asp Asp Pro Phe Ser Gly Lys  
2090 2095 2100

Thr Val Ser Val Ser Glu Ala Ile Lys Lys Asn Leu Ile Asp Arg  
2105 2110 2115

Glu Thr Gly Met Arg Leu Leu Glu Ala Gln Ile Ala Ser Gly Gly  
2120 2125 2130

Val Val Asp Pro Val Asn Ser Val Phe Leu Pro Lys Asp Val Ala  
2135 2140 2145



Leu Ala Arg Gly Leu Ile Asp Arg Asp Leu Tyr Arg Ser Leu Asn  
2150 2155 2160  
Asp Pro Arg Asp Ser Gln Lys Asn Phe Val Asp Pro Val Thr Lys  
2165 2170 2175  
Lys Lys Val Ser Tyr Val Gln Leu Lys Glu Arg Cys Arg Ile Glu  
2180 2185 2190 2195  
Pro His Thr Gly Leu Leu Leu Leu Ser Val Gln Lys Arg Ser Met  
2200 2205  
Ser Phe Gln Gly Ile Arg Gln Pro Val Thr Val Thr Glu Leu Val  
2210 2215 2220  
Asp Ser Gly Ile Leu Arg Pro Ser Thr Val Asn Glu Leu Glu Ser  
2225 2230 2235  
Gly Gln Ile Ser Tyr Asp Glu Val Gly Glu Arg Ile Lys Asp Phe  
2240 2245 2250  
Leu Gln Gly Ser Ser Cys Ile Ala Gly Ile Tyr Asn Glu Thr Thr  
2255 2260 2265  
Lys Gln Lys Leu Gly Ile Tyr Glu Ala Met Lys Ile Gly Leu Val  
2270 2275 2280  
Arg Pro Gly Thr Ala Leu Glu Leu Leu Glu Ala Gln Ala Ala Thr  
2285 2290 2295  
Gly Phe Ile Val Asp Pro Val Ser Asn Leu Arg Leu Pro Val Glu  
2300 2305 2310  
Glu Ala Tyr Lys Arg Gly Leu Val Gly Ile Glu Phe Lys Glu Lys  
2315 2320 2325  
Leu Leu Ser Ala Glu Arg Ala Val Thr Gly Tyr Asn Asp Pro Glu  
2330 2335 2340  
Thr Gly Asn Ile Ile Ser Leu Phe Gln Ala Met Asn Lys Glu Leu  
2345 2350 2355  
Ile Glu Lys Gly His Gly Ile Arg Leu Leu Glu Ala Gln Ile Ala  
2360 2365 2370  
Thr Gly Gly Ile Ile Asp Pro Lys Glu Ser His Arg Leu Pro Val  
2375 2380 2385  
Asp Ile Ala Tyr Lys Arg Gly Tyr Phe Asn Glu Glu Leu Ser Glu  
2390 2395 2400  
Ile Leu Ser Asp Pro Ser Asp Asp Thr Lys Gly Phe Phe Asp Pro  
2405 2410 2415  
Asn Thr Glu Glu Asn Leu Thr Tyr Leu Gln Leu Lys Glu Arg Cys  
2420 2425 2430  
Ile Lys Asp Glu Glu Thr Gly Leu Cys Leu Leu Pro Leu Lys Glu  
2435 2440 2445

Lys Lys Lys Gln Val Gln Thr Ser Gln Lys Asn Thr Leu Arg Lys  
2450 2455 2460  
Arg Arg Val Val Ile Val Asp Pro Glu Thr Asn Lys Glu Met Ser  
2465 2470 2475  
Val Gln Glu Ala Tyr Lys Lys Gly Leu Ile Asp Tyr Glu Thr Phe  
2480 2485 2490  
Lys Glu Leu Cys Glu Gln Glu Cys Glu Trp Glu Glu Ile Thr Ile  
2495 2500 2505  
Thr Gly Ser Asp Gly Ser Thr Arg Val Val Leu Val Asp Arg Lys  
2510 2515 2520  
Thr Gly Ser Gln Tyr Asp Ile Gln Asp Ala Ile Asp Lys Gly Leu  
2525 2530 2535  
Val Asp Arg Lys Phe Phe Asp Gln Tyr Arg Ser Gly Ser Leu Ser  
2540 2545 2550  
Leu Thr Gln Phe Ala Asp Met Ile Ser Leu Lys Asn Gly Val Gly  
2555 2560 2565  
Thr Ser Ser Ser Met Gly Ser Gly Val Ser Asp Asp Val Phe Ser  
2570 2575 2580  
Ser Ser Arg His Glu Ser Val Ser Lys Ile Ser Thr Ile Ser Ser  
2585 2590 2595  
Val Arg Asn Leu Thr Ile Arg Ser Ser Ser Phe Ser Asp Thr Leu  
2600 2605 2610  
Glu Glu Ser Ser Pro Ile Ala Ala Ile Phe Asp Thr Glu Asn Leu  
2615 2620 2625  
Glu Lys Ile Ser Ile Thr Glu Gly Ile Glu Arg Gly Ile Val Asp  
2630 2635 2640  
Ser Ile Thr Gly Gln Arg Leu Leu Glu Ala Gln Ala Cys Thr Gly  
2645 2650 2655  
Gly Ile Ile His Pro Thr Thr Gly Gln Lys Leu Ser Leu Gln Asp  
2660 2665 2670  
Ala Val Ser Gln Gly Val Ile Asp Gln Asp Met Ala Thr Ser Val  
2675 2680 2685  
Lys Pro Ala Gln Lys Ala Phe Ile Gly Phe Glu Gly Val Lys Gly  
2690 2695 2700  
Lys Lys Lys Met Ser Ala Ala Glu Ala Val Lys Glu Lys Trp Leu  
2705 2710 2715  
Pro Tyr Glu Ala Gly Gln Arg Phe Leu Glu Phe Gln Tyr Leu Thr  
2720 2725 2730  
Gly Gly Leu Val Asp Pro Glu Val His Gly Arg Ile Ser Thr Glu  
2735 2740 2745

Glu Ala Ile Arg Lys Gly Phe Ile Asp Gly Arg Ala Ala Gln Arg  
2750 2755 2760

Leu Gln Asp Thr Ser Ser Tyr Ala Lys Ile Leu Thr Cys Pro Lys  
2765 2770 2775

Thr Lys Leu Lys Ile Ser Tyr Lys Asp Ala Ile Asn Arg Ser Met  
2780 2785 2790

Val Glu Asp Ile Thr Gly Leu Arg Leu Leu Glu Ala Ala Ser Val  
2795 2800 2805

Ser Ser Lys Gly Leu Pro Ser Pro Tyr Asn Met Ser Ser Ala Pro  
2810 2815 2820

Gly Ser Arg Ser Gly Ser Arg Ser Gly Ser Arg Ser Gly Ser Arg  
2825 2830 2835

Ser Gly Ser Arg Ser Gly Ser Arg Arg Gly Ser Phe Asp Ala Thr  
2840 2845 2850

Gly Asn Ser Ser Tyr Ser Tyr Ser Tyr Ser Phe Ser Ser Ser Ser  
2855 2860 2865

Ile Gly His  
2870

<210> 113  
<211> 381  
<212> PRT  
<213> Homo sapiens  
<400> 113

Met Trp Arg Leu Met Ser Arg Phe Asn Ala Phe Lys Arg Thr Asn Thr  
1 5 10 15

Ile Leu His His Leu Arg Met Ser Lys His Thr Asp Ala Ala Glu Glu  
20 25 30

Val Leu Leu Glu Lys Lys Gly Cys Ala Gly Val Ile Thr Leu Asn Arg  
35 40 45

Pro Lys Phe Leu Asn Ala Leu Thr Leu Asn Met Ile Arg Gln Ile Tyr  
50 55 60

Pro Gln Leu Lys Lys Trp Glu Gln Asp Pro Glu Thr Phe Val Ile Ile  
65 70 75 80

Ile Lys Gly Ala Gly Gly Lys Ala Phe Cys Ala Gly Gly Asp Ile Arg  
85 90 95

Val Ile Ser Glu Ala Glu Lys Ala Lys Gln Lys Ile Ala Pro Val Phe  
100 105 110

Phe Arg Glu Glu Tyr Met Leu Asn Asn Ala Val Gly Ser Cys Gln Lys  
115 120 125

Pro Tyr Val Ala Leu Ile His Gly Ile Thr Met Gly Gly Val Gly  
130 135 140

Leu Ser Val His His Gly Gln Phe Arg Val Ala Thr Glu Lys Cys Leu Phe  
145 150 155

Ala Met Pro Glu Thr Ala Ile Gly Leu Phe Pro Asp Val Gly Gly Gly  
165 170 175

Tyr Phe Phe Ala Thr Thr Pro Arg Lys Thr Trp Leu Leu Pro Cys Ile  
180 185 190

Asn Gly Phe Arg Leu Lys Gly Arg Asp Val Tyr Arg Ala Gly Ile Ala  
195 200 205

Thr His Phe Val Asp Ser Glu Lys Leu Ala Met Leu Glu Glu Asp Leu  
210 215 220

Leu Ala Leu Lys Ser Pro Ser Lys Glu Asn Ile Ala Ser Val Leu Glu  
225 230 235 240

Asn Tyr His Thr Glu Ser Lys Ile Asp Arg Asp Lys Ser Phe Ile Leu  
245 250 255

Glu Glu His Met Asp Lys Ile Asn Ser Cys Phe Ser Ala Asn Thr Val  
260 265 270

Glu Glu Ile Ile Glu Asn Leu Gln Gln Asp Gly Ser Ser Phe Ala Leu  
275 280 285

Glu Gln Leu Lys Val Ile Asn Lys Met Ser Pro Thr Ser Leu Lys Ile  
290 295 300

Thr Leu Arg Gln Leu Met Glu Gly Ser Ser Lys Thr Leu Gln Glu Val  
305 310 315 320

Leu Thr Met Glu Tyr Arg Leu Ser Gln Ala Cys Met Arg Gly His Asp  
325 330 335

Phe His Glu Gly Val Arg Ala Val Leu Ile Asp Lys Asp Gln Ser Pro  
340 345 350

Lys Trp Lys Pro Ala Asp Leu Lys Glu Val Thr Glu Glu Asp Leu Asn  
355 360 365

Asn His Phe Lys Ser Leu Gly Ser Ser Asp Leu Lys Phe  
370 375 380

<210> 114  
<211> 1139  
<212> PRT  
<213> Homo sapiens  
<400> 114

Met Gln Thr Pro Glu Val Pro Ala Glu Arg Ser Pro Arg Arg Arg Ser  
1 5 10 15

Ile Ser Gly Thr Ser Thr Ser Glu Lys Pro Asn Ser Met Asp Thr Ala  
20 25 30

Asn Thr Ser Pro Phe Lys Val Pro Gly Phe Phe Ser Lys Arg Leu Lys  
35 40 45

Gly Ser Ile Lys Arg Thr Lys Ser Gln Ser Lys Leu Asp Arg An Thr  
50 55 60

Ser Phe Arg Leu Pro Ser Leu Arg Ser Thr Asp Asp Arg Ser Arg Gly  
65 70 75 80

Leu Pro Lys Leu Lys Glu Ser Arg Ser His Glu Ser Leu Leu Ser Pro  
85 90 95

Cys Ser Thr Val Glu Cys Leu Asp Leu Gly Arg Gly Glu Pro Val Ser  
100 105 110

Val Lys Pro Leu His Ser Ser Ile Leu Gly Gln Asp Phe Cys Phe Glu  
115 120 125

Val Thr Tyr Leu Ser Gly Ser Lys Cys Phe Ser Cys An Ser Ala Ser  
130 135 140

Glu Arg Asp Lys Trp Met Glu Asn Leu Arg Arg Thr Val Gln Pro An  
145 150 155 160

Lys Asp Asn Cys Arg Arg Ala Glu Asn Val Leu Arg Leu Trp Ile Ile  
165 170 175

Glu Ala Lys Asp Leu Ala Pro Lys Lys Tyr Phe Cys Glu Leu Cys  
180 185 190

Leu Asp Asp Thr Leu Phe Ala Arg Thr Thr Ser Lys Thr Lys Ala Asp  
195 200 205

An Ile Phe Trp Gly Glu His Phe Glu Phe Ser Leu Pro Pro Leu  
210 215 220

His Ser Ile Thr Val His Ile Tyr Lys Asp Val Glu Lys Lys Lys  
225 230 235 240

Lys Asp Lys Asn Asn Tyr Val Gly Leu Val An Ile Pro Thr Ala Ser  
245 250 255

Val Thr Gly Arg Gln Phe Val Glu Lys Trp Tyr Pro Val Ser Thr Pro  
260 265 270

Thr Pro An Lys Gly Lys Thr Gly Gly Pro Ser Ile Arg Ile Lys Ser  
275 280 285

Arg Phe Gln Thr Ile Thr Ile Leu Pro Met Glu Gln Tyr Lys Glu Phe  
290 295 300

Ala Glu Phe Val Thr Ser Asn Tyr Thr Met Leu Cys Ser Val Leu Glu  
305 310 315 320

Pro Val Ile Ser Val Arg An Lys Glu Leu Ala Cys Ala Leu Val  
325 330 335

His Ile Leu Gln Ser Thr Gly Arg Ala Lys Asp Phe Leu Thr Asp Leu  
340 345 350

Val Met Ser Glu Val Asp Arg Cys Gly Glu His Asp Val Leu Ile Phe

Arg Glu An Thr Ile Ala Thr Lys Ser Ile Glu Glu Tyr Leu Lys Leu  
355 360 365 370

Val Gly Gln Gln Tyr Leu His Asp Ala Leu Glu Glu Phe Ile Lys Ala  
385 390 395 400

Leu Tyr Glu Ser Asp Glu An Cys Glu Val Asp Pro Ser Lys Cys Ser  
405 410 415

Ser Ser Glu Leu Ile Asp His Gln Ser An Leu Lys Met Cys Cys Glu  
420 425 430

Leu Ala Phe Cys Lys Ile Ile An Ser Tyr Cys Val Phe Pro Arg Glu  
435 440 445

Leu Lys Glu Val Phe Ala Ser Trp Lys Gln Gln Cys Leu An Arg Gly  
450 455 460

Lys Gln Asp Ile Ser Glu Arg Leu Ile Ser Ala Ser Leu Phe Leu Arg  
465 470 475 480

Phe Leu Cys Pro Ala Ile Met Ser Pro Ser Leu Phe An Leu Met Gln  
485 490 495

Glu Tyr Pro Asp Asp Arg Thr Ser Arg Thr Leu Thr Leu Ile Ala Lys  
500 505 510

Val Ile Gln An Leu Ala An Phe Ala Lys Phe Gly An Lys Glu Glu  
515 520 525

Tyr Met Ala Phe Met An Asp Phe Leu Glu His Glu Trp Gly Gly Met  
530 535 540

Lys Arg Phe Leu Leu Glu Ile Ser An Pro Asp Thr Ile Ser An Thr  
545 550 555 560

Pro Gly Phe Asp Gly Tyr Ile Asp Leu Glu Arg Glu Leu Ser Val Leu  
565 570 575

His Ser Leu Leu Trp Glu Val Val Ser Gln Leu Asp Lys Gly Glu An  
580 585 590

Ser Phe Leu Gln Ala Thr Val Ala Lys Leu Gly Pro Leu Pro Arg Val  
595 600 605

Leu Ala Asp Ile Thr Lys Ser Leu Thr An Pro Thr Pro Ile Gln Gln  
610 615 620

Gln Leu Arg Arg Phe Thr Glu His An Ser Ser Pro An Val Ser Gly  
625 630 635 640

Ser Leu Ser Ser Gly Leu Gln Lys Ile Phe Glu Asp Pro Thr Asp Ser  
645 650 655

Asp Leu His Lys Leu Lys Ser Pro Ser Gln Asp An Thr Asp Ser Tyr  
660 665 670

Phe Arg Gly Lys Thr Leu Leu Val Gln Ala Ser Ser Gln Ser 685  
 675  
 Met Thr Tyr Ser Glu Lys Asp Glu Arg Ser Ser Leu Pro Asn Gly 700  
 690  
 Arg Ser Val Ser Leu Met Asp Leu Gln Asp Thr His Ala Ala Gln Val 720  
 705  
 Glu His Ala Ser Val Met Leu Asp Val Pro Ile Arg Leu Thr Gly Ser 735  
 725  
 Gln Leu Ser Ile Thr Gln Val Ala Ser Ile Lys Gln Leu Arg Glu Thr 750  
 740  
 Gln Ser Thr Pro Gln Ser Ala Pro Gln Val Arg Arg Pro Leu His Pro 765  
 755  
 Ala Leu Asn Gln Pro Gly Gly Leu Gln Pro Leu Ser Phe Gln Asn Pro 780  
 770  
 Val Tyr His Leu Asn Asn Pro Ile Pro Ala Met Pro Lys Ala Ser Ile 800  
 785  
 Asp Ser Ser Leu Glu Asn Leu Ser Thr Ala Ser Ser Arg Ser Gln Ser 815  
 805  
 Asn Ser Glu Asp Phe Lys Leu Ser Gly Pro Ser Asn Ser Ser Met Glu 830  
 820  
 Asp Phe Thr Lys Arg Ser Thr Gln Ser Glu Asp Phe Ser Arg Arg His 845  
 835  
 Thr Val Pro Asp Arg His Ile Pro Leu Ala Leu Pro Arg Gln Asn Ser 860  
 850  
 Thr Gly Gln Ala Gln Ile Arg Lys Val Asp Gln Gly Gly Leu Gly Ala 880  
 865  
 Arg Ala Lys Ala Pro Ser Leu Pro His Ser Ala Ser Leu Arg Ser 895  
 885  
 Thr Gly Ser Met Ser Val Val Ser Ala Ala Leu Val Ala Glu Pro Val 910  
 900  
 Gln Asn Gly Ser Arg Ser Arg Gln Gln Ser Ser Ser Ser Arg Glu Ser 925  
 915  
 Pro Val Pro Lys Val Arg Ala Ile Gln Arg Gln Gln Thr Gln Gln Val 940  
 930  
 Gln Ser Pro Val Asp Ser Ala Thr Met Ser Pro Pro Val Glu Arg Thr Ala 960  
 945  
 Ala Trp Val Leu Asn Asn Gly Gln Tyr Glu Glu Asp Val Glu Glu Thr 975  
 965  
 Glu Gln Asn Leu Asp Glu Ala Lys His Ala Glu Lys Tyr Glu Gln Glu 990  
 980

Ile Thr Lys Leu Lys Glu Arg Leu Arg Val Ser Ser Arg Arg Leu Glu 1005  
 995  
 Glu Tyr Glu Arg Arg Leu Leu Val Gln Glu Gln Gln Met Gln Lys 1020  
 1010  
 Leu Leu Leu Glu Tyr Lys Ala Arg Leu Glu Asp Ser Glu Glu Arg 1035  
 1025  
 Leu Arg Arg Gln Gln Glu Glu Lys Asp Ser Gln Met Lys Ser Ile 1050  
 1040  
 Ile Ser Arg Leu Met Ala Val Glu Glu Glu Leu Lys Lys Asp His 1065  
 1055  
 Ala Glu Met Gln Ala Val Ile Asp Ala Lys Gln Lys Ile Ile Asp 1080  
 1070  
 Ala Gln Glu Lys Arg Ile Val Ser Leu Asp Ser Ala Asn Thr Arg 1095  
 1085  
 Leu Met Ser Ala Leu Thr Gln Val Lys Glu Arg Tyr Ser Met Gln 1110  
 1100  
 Val Arg Asn Gly Ile Ser Pro Thr Asn Pro Thr Lys Leu Ser Ile 1125  
 1115  
 Thr Glu Asn Gly Glu Phe Lys Asn Ser Ser Cys 1135  
 1130  
 <210> 115  
 <211> 185  
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 <213> Homo sapiens  
 <400> 115  
 Met Thr Leu Glu Glu Phe Ser Ala Gly Glu Gln Lys Thr Glu Arg Met 1  
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 Asp Lys Val Gly Asp Ala Leu Glu Glu Val Leu Ser Lys Ala Leu Ser 30  
 20  
 Gln Arg Thr Ile Thr Val Gly Val Tyr Glu Ala Ala Lys Leu Leu Asn 45  
 35  
 Val Asp Pro Asp Asn Val Val Leu Cys Leu Leu Ala Ala Asp Glu Asp 60  
 50  
 Asp Asp Arg Asp Val Ala Leu Gln Ile His Phe Thr Leu Ile Gln Ala 80  
 65  
 Phe Cys Cys Glu Asn Asp Ile Asn Ile Leu Arg Val Ser Asn Pro Gly 95  
 85  
 Arg Leu Ala Glu Leu Leu Leu Leu Thr Asp Ala Gly Pro Ala Ala 110  
 100  
 Ser Glu Gly Ala Glu Gln Pro Pro Asp Leu His Cys Val Leu Val Thr 125  
 115

Asn Pro His Ser Ser Gln Trp Lys Asp Pro Ala Leu Ser Gln Leu Ile  
130 135 140

Cys Phe Cys Arg Glu Ser Arg Tyr Met Asp Gln Trp Val Pro Val Ile  
145 150 155 160

Asn Leu Pro Glu Arg  
165

<210> 116

<211> 1163

<212> PRT

<213> Homo sapiens

<400> 116

Met Thr Arg Thr Arg Ala Ala Leu Leu Leu Phe Thr Ala Leu Ala Thr  
1 5 10 15

Ser Leu Gly Phe Asn Leu Asp Thr Glu Glu Leu Thr Ala Phe Arg Val  
20 25 30

Asp Ser Ala Gly Phe Gly Asp Ser Val Val Gln Tyr Ala Asn Ser Trp  
35 40 45

Val Val Val Gly Ala Pro Gln Lys Ile Thr Ala Ala Asn Gln Thr Gly  
50 55 60

Gly Leu Tyr Gln Cys Gly Tyr Ser Thr Gly Ala Cys Glu Pro Ile Gly  
65 70 75 80

Leu Gln Val Pro Gln Ala Val Asn Met Ser Leu Gly Leu Ser Leu  
85 90 95

Ala Ser Thr Thr Ser Pro Ser Gln Leu Leu Ala Cys Gly Pro Thr Val  
100 105 110

His His Glu Cys Gly Arg Asn Met Tyr Leu Thr Gly Leu Cys Phe Leu  
115 120 125

Leu Gly Pro Thr Gln Leu Thr Gln Arg Leu Pro Val Ser Arg Gln Glu  
130 135 140

Cys Pro Arg Gln Glu Gln Asp Ile Val Phe Leu Ile Asp Gly Ser Gly  
145 150 155 160

Ser Ile Ser Ser Arg Asn Phe Ala Thr Met Met Asn Phe Val Arg Ala  
165 170 175

Val Ile Ser Gln Phe Gln Arg Pro Ser Thr Gln Phe Ser Leu Met Gln  
180 185 190

Phe Ser Asn Lys Phe Gln Thr His Leu Thr Phe Glu Glu Phe Arg Arg  
195 200 205

Thr Ser Asn Pro Leu Ser Leu Leu Ala Ser Val His Gln Leu Gln Gly  
210 215 220

Phe Thr Tyr Thr Ala Thr Ala Ile Gln Asn Val Val His Arg Leu Phe  
225 230 235 240

His Ala Ser Tyr Gly Ala Arg Arg Asp Ala Thr Lys Ile Leu Ile Val  
245 250 255

Ile Thr Asp Gly Lys Lys Glu Gly Asp Thr Leu Asp Tyr Lys Asp Val  
260 265 270

Ile Pro Met Ala Asp Ala Ala Gly Ile Ile Arg Tyr Ala Ile Gly Val  
275 280 285

Gly Leu Ala Phe Gln Asn Arg Asn Ser Trp Lys Glu Leu Asn Asp Ile  
290 295 300

Ala Ser Lys Pro Ser Ser Gln Glu His Ile Phe Lys Val Glu Asp Phe Asp  
305 310 315 320

Ala Leu Lys Asp Ile Gln Thr Gln Leu Arg Glu Lys Ile Phe Pro Ile  
325 330 335

Glu Gly Thr Glu Thr Thr Ser Ser Ser Phe Glu Leu Glu Met Ala  
340 345 350

Gln Glu Gly Phe Ser Ala Val Phe Thr Pro Asp Gly Pro Val Leu Gly  
355 360 365

Ala Val Gly Ser Phe Thr Trp Ser Gly Gly Ala Phe Leu Tyr Pro Pro  
370 375 380

Asn Met Ser Pro Thr Phe Ile Asn Met Ser Ser Gln Glu Asn Val Asp Met  
385 390 395 400

Arg Asp Ser Tyr Leu Gly Tyr Ser Thr Glu Leu Ala Leu Trp Lys Gly  
405 410 415

Val Gln Ser Leu Val Leu Gly Ala Pro Arg Tyr Gln His Thr Gly Lys  
420 425 430

Ala Val Ile Phe Thr Gln Val Ser Arg Gln Trp Arg Met Lys Ala Glu  
435 440 445

Val Thr Gly Thr Gln Ile Gly Ser Tyr Phe Gly Pro Ser Leu Cys Ser  
450 455 460

Val Asp Val Asp Ser Asp Gly Ser Thr Asp Leu Val Leu Ile Gly Pro  
465 470 475 480

Pro His Tyr Tyr Glu Gln Thr Arg Gly Ala Gln Val Ser Val Cys Pro  
485 490 495

Leu Pro Arg Gly Trp Arg Trp Trp Cys Asp Ala Val Leu Tyr Gly  
500 505 510

Glu Gln Gly His Pro Trp Gly Arg Phe Gly Ala Ala Leu Thr Val Leu  
515 520 525

Gly Asp Val Asn Gly Asp Lys Leu Thr Asp Val Val Ile Gly Ala Pro  
530 535 540

Gly Glu Glu Asn Arg Gly Ala Val Tyr Leu Phe His Gly Val Leu  
545 550 555 560

Gly Pro Ser Ile Ser Pro Ser His Ser Gln Arg Ile Ala Gly Ser Gln  
565 570 575

Leu Ser Ser Arg Leu Gln Tyr Phe Gly Gln Ala Leu Ser Gly Gly Gln  
580 585 590

Asp Leu Thr Gln Asp Gly Leu Val Asp Leu Ala Val Gly Ala Arg Gly  
595 600 605

Gln Val Leu Leu Arg Thr Arg Pro Val Leu Trp Val Gly Val Ser  
610 615 620

Met Gln Phe Ile Pro Ala Glu Ile Pro Arg Ser Ala Phe Glu Cys Arg  
625 630 635

Glu Gln Val Val Ser Glu Gln Thr Leu Val Gln Ser Asn Ile Cys Leu  
645 650 655

Tyr Ile Asp Lys Arg Ser Lys Asn Leu Leu Gly Ser Arg Asp Leu Gln  
660 665 670

Ser Ser Val Thr Leu Asp Leu Ala Leu Asp Pro Gly Arg Leu Ser Pro  
675 680 685

Arg Ala Thr Phe Gln Glu Thr Lys Asn Arg Ser Leu Ser Arg Val Arg  
690 695 700

Val Leu Gly Leu Lys Ala His Cys Glu Asn Phe Asn Leu Leu Leu Pro  
705 710 715

Ser Cys Val Glu Asp Ser Val Thr Pro Ile Thr Leu Arg Leu Asn Phe  
725 730 735

Thr Leu Val Gly Lys Pro Leu Leu Ala Phe Arg Asn Leu Arg Pro Met  
740 745 750

Leu Ala Ala Asp Ala Gln Arg Tyr Phe Thr Ala Ser Leu Pro Phe Glu  
755 760 765

Lys Asn Cys Gly Ala Asp His Ile Cys Gln Asp Asn Leu Gly Ile Ser  
770 775 780

Phe Ser Phe Pro Gly Leu Lys Ser Leu Leu Val Gly Ser Asn Leu Glu  
785 790 795

Leu Asn Ala Glu Val Met Val Trp Asn Asp Gly Glu Asp Ser Tyr Gly  
805 810 815

Thr Thr Ile Thr Phe Ser His Pro Ala Gly Leu Ser Tyr Arg Tyr Val  
820 825 830

Ala Glu Gly Gln Lys Gln Gly Glu Leu Arg Ser Leu His Leu Thr Cys  
835 840 845

Asp Ser Ala Pro Val Gly Ser Gln Gly Thr Trp Ser Thr Ser Cys Arg  
850 855 860

Ile Asn His Leu Ile Phe Arg Gly Gly Ala Gln Ile Thr Phe Leu Ala

865 870 875 880

Thr Phe Asp Val Ser Pro Lys Ala Val Leu Gly Asp Arg Leu Leu Leu  
885 890 895

Thr Ala Asn Val Ser Ser Glu Asn Asn Thr Pro Arg Thr Ser Lys Thr  
900 905 910

Thr Phe Gln Leu Glu Leu Pro Val Lys Tyr Ala Val Tyr Thr Val Val  
915 920 925

Ser Ser His Glu Gln Phe Thr Lys Tyr Leu Asn Phe Ser Glu Ser Glu  
930 935 940

Glu Lys Glu Ser His Val Ala Met His Arg Tyr Gln Val Asn Asn Leu  
945 950 955

Gly Gln Arg Asp Leu Pro Val Ser Ile Asn Phe Trp Val Pro Val Glu  
965 970 975

Leu Asn Gln Glu Ala Val Trp Met Asp Val Glu Val Ser Leu Pro Gln  
980 985 990

Asn Pro Ser Leu Arg Cys Ser Ser Glu Lys Ile Ala Gly Pro Ala Ser  
995 1000 1005

Asp Phe Leu Ala His Ile Gln Lys Asn Pro Val Leu Asp Cys Ser  
1010 1015 1020

Ile Ala Gly Cys Leu Arg Phe Arg Cys Asp Val Pro Ser Phe Ser  
1025 1030 1035

Val Gln Glu Glu Leu Asp Phe Thr Leu Lys Gly Asn Leu Ser Phe  
1040 1045 1050

Gly Trp Val Arg Gln Ile Leu Gln Lys Lys Val Ser Val Val Ser  
1055 1060 1065

Val Ala Glu Ile Thr Phe Asp Thr Ser Val Tyr Ser Gln Leu Pro  
1070 1075 1080

Gly Gln Glu Ala Phe Met Arg Ala Gln Thr Thr Thr Val Leu Glu  
1085 1090 1095

Lys Tyr Lys Val His Asn Pro Thr Pro Leu Ile Val Gly Ser Ser  
1100 1105 1110

Ile Gly Gly Leu Leu Leu Leu Ala Leu Ile Thr Ala Val Leu Tyr  
1115 1120 1125

Lys Val Gly Phe Phe Lys Arg Gln Tyr Lys Glu Met Met Glu Glu  
1130 1135 1140

Ala Asn Gly Gln Ile Ala Pro Glu Asn Gly Thr Gln Thr Pro Ser  
1145 1150 1155

Pro Pro Ser Glu Lys  
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Lys Gly Leu Glu Leu Arg Lys Thr Val Thr Thr Val Glu Thr Gln Asn  
35 40 45  
Leu Glu Gly Leu His His Asp Gly Gln Phe Cys His Lys Pro Cys Pro  
50 55 60  
Pro Gly Glu Arg Lys Ala Arg Asp Cys Thr Val Asn Gly Asp Glu Pro  
65 70 75 80  
Asp Cys Val Pro Cys Gln Glu Gly Lys Glu Tyr Thr Asp Lys Ala His  
85 90 95  
Phe Ser Ser Lys Cys Arg Arg Cys Arg Leu Cys Asp Glu Gly His Gly  
100 105 110  
Leu Glu Val Glu Ile Asn Cys Thr Arg Thr Gln Asn Thr Lys Cys Arg  
115 120 125  
Cys Lys Pro Asn Phe Cys Asn Ser Thr Val Cys Glu His Cys Asp  
130 135 140  
Pro Cys Thr Lys Cys Glu His Gly Ile Ile Lys Glu Cys Thr Leu Thr  
145 150 155  
Ser Asn Thr Lys Cys Lys Glu Glu Gly Ser Arg Ser Asn Leu Gly Trp  
160 165 170 175  
Leu Cys Leu Leu Leu Leu Pro Ile Pro Leu Ile Val Trp Val Lys Arg  
180 185 190  
Lys Glu Val Gln Lys Thr Cys Arg Lys His Arg Lys Glu Asn Gln Gly  
195 200 205  
Ser His Glu Ser Pro Thr Leu Asn Pro Glu Thr Val Ala Ile Asn Leu  
210 215 220  
Ser Asp Val Asp Leu Ser Lys Tyr Ile Thr Thr Ile Ala Gly Val Met  
225 230 235 240  
Thr Leu Ser Gln Val Lys Gly Phe Val Arg Lys Asn Gly Val Asn Glu  
245 250 255  
Ala Lys Ile Asp Glu Ile Lys Asn Asp Asn Val Gln Asp Thr Ala Glu  
260 265 270  
Gln Lys Val Gln Leu Leu Arg Asn Trp His Gln Leu His Gly Lys Lys  
275 280 285

Glu Ala Tyr Asp Thr Leu Ile Lys Asp Leu Lys Lys Ala Asn Leu Cys  
290 295  
Thr Leu Ala Glu Lys Ile Gln Thr Ile Ile Leu Lys Asp Ile Thr Ser  
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Asp Ser Glu Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val  
325 330 335  
<210> 118  
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20 25 30  
Pro Gln Arg Leu Leu Trp Gln Thr Ala Val Arg His Ile Thr Glu Gln  
35 40 45  
Arg Phe Ile His Gly His Arg Gly Gly Ser Gly Ser Gly Ser Gly Gly  
50 55 60  
Ser Gly Lys Ala Ser Asp Pro Ala Gly Gly Pro Asn His His Ala  
65 70 75 80  
Pro Gln Leu Ser Gly Asp Ser Ala Leu Pro Leu Tyr Ser Leu Gly Pro  
85 90 95  
Gly Glu Arg Ala His Ser Thr Cys Gly Thr Lys Val Phe Pro Glu Arg  
100 105 110  
Ser Gly Ser Gly Ser Ala Ser Gly Ser Gly Gly Gly Asp Leu Gly  
115 120 125  
Phe Leu His Leu Asp Cys Ala Pro Ser Asn Ser Asp Phe Leu Asn  
130 135 140  
Gly Gly Tyr Ser Tyr Arg Gly Val Ile Phe Pro Thr Leu Arg Asn Ser  
145 150 155 160  
Phe Lys Ser Arg Asp Leu Glu Arg Leu Tyr Gln Arg Tyr Phe Leu Gly  
165 170 175  
Gln Arg Arg Lys Ser Glu Val Val Met Asn Val Leu Asp Val Leu Thr  
180 185 190  
Lys Leu Thr Leu Leu Val Leu His Leu Ser Leu Ala Ser Ala Pro Met  
195 200 205  
Asp Pro Leu Lys Gly Ile Leu Leu Gly Phe Phe Thr Gly Ile Glu Val  
210 215 220  
Val Ile Cys Ala Leu Val Val Arg Lys Asp Thr Thr Ser His Thr  
225 230 235 240

Tyr Leu Gln Tyr Ser Gly Val Val Thr Trp Val Ala Met Thr Thr Gln 235  
 245  
 Ile Leu Ala Ala Gly Leu Gly Tyr Gly Leu Leu Gly Asp Gly Ile Gly 270  
 280  
 Tyr Val Leu Phe Thr Leu Phe Ala Thr Tyr Ser Met Leu Pro Leu Pro 285  
 275  
 Leu Thr Trp Ala Ile Leu Ala Gly Leu Gly Thr Ser Leu Leu Gln Val 300  
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 Ile Leu Gln Val Val Ile Pro Arg Leu Ala Val Ile Ser Ile Asn Gln 320  
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 Val Val Ala Gln Ala Val Leu Phe Met Cys Met Asn Thr Ala Gly Ile 335  
 325  
 Phe Ile Ser Tyr Leu Ser Asp Arg Ala Gln Arg Gln Ala Phe Leu Glu 350  
 340  
 Thr Arg Arg Cys Val Gln Ala Arg Leu Arg Leu Glu Thr Gln Asn Gln 365  
 355  
 Arg Gln Gln Arg Leu Val Leu Ser Val Leu Pro Arg Phe Val Val Leu 380  
 370  
 Glu Met Ile Asn Asp Met Thr Asn Val Glu Asp Glu His Leu Gln His 400  
 385  
 Gln Phe His Arg Ile Tyr Ile His Arg Tyr Gln Asn Val Ser Ile Leu 415  
 405  
 Phe Ala Asp Val Lys Gly Phe Thr Asn Leu Ser Thr Thr Leu Ser Ala 430  
 420  
 Gln Gln Leu Val Arg Met Leu Asn Gln Leu Phe Ala Arg Phe Asp Arg 445  
 435  
 Leu Ala His Gln His His Cys Leu Arg Ile Lys Ile Leu Gly Asp Cys 460  
 450  
 Tyr Tyr Cys Val Ser Gly Leu Pro Glu Pro Arg Gln Asp His Ala His 480  
 465  
 Cys Cys Val Gln Met Gly Leu Ser Met Ile Lys Thr Ile Arg Tyr Val 495  
 485  
 Arg Ser Arg Thr Lys His Asp Val Asp Met Arg Ile Gly Ile His Ser 510  
 500  
 Gly Ser Val Leu Cys Gly Val Leu Gly Leu Arg Lys Trp Gln Phe Asp 525  
 515  
 Val Trp Ser Trp Asp Val Asp Ile Ala Asn Lys Leu Glu Ser Gly Gly 540  
 530  
 Ile Pro Gly Arg Ile His Ile Ser Lys Ala Thr Leu Asp Cys Leu Asn 560  
 545

Gly Asp Tyr Asn Val Glu Glu Gly His Gly Lys Glu Arg Asn Glu Phe 575  
 565  
 Leu Arg Lys His Asn Ile Glu Thr Tyr Leu Ile Lys Gln Pro Glu Asp 590  
 580  
 Ser Leu Leu Ser Leu Pro Glu Asp Ile Val Lys Glu Ser Val Ser Ser 605  
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 Ser Asp Arg Arg Asn Ser Gly Ala Thr Phe Thr Glu Gly Ser Trp Ser 620  
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 Pro Glu Leu Pro Phe Asp Asn Ile Val Gly Lys Gln Asn Thr Leu Ala 640  
 625  
 Ala Leu Thr Arg Asn Ser Ile Asn Leu Leu Pro Asn His Leu Ala Gln 655  
 645  
 Ala Leu His Val Gln Ser Gly pro Glu Glu Ile Asn Lys Arg Ile Glu 670  
 660  
 His Thr Ile Asp Leu Arg Ser Gly Asp Lys Leu Arg Arg Glu His Ile 685  
 675  
 Lys Pro Phe Ser Leu Met Phe Lys Asp Ser Ser Leu Glu His Lys Tyr 700  
 690  
 Ser Gln Met Arg Asp Glu Val Phe Lys Ser Asn Leu Val Cys Ala Phe 720  
 705  
 Ile Val Leu Leu Phe Ile Thr Ala Ile Gln Ser Leu Leu Pro Ser Ser 735  
 725  
 Arg Val Met Pro Met Thr Ile Gln Phe Ser Ile Leu Ile Met Leu His 750  
 740  
 Ser Ala Leu Val Leu Ile Thr Thr Ala Glu Asp Tyr Lys Cys Leu Pro 765  
 755  
 Leu Ile Leu Arg Lys Thr Cys Cys Trp Ile Asn Glu Thr Tyr Leu Ala 780  
 770  
 Arg Asn Val Ile Ile Phe Ala Ser Ile Leu Ile Asn Phe Leu Gly Ala 800  
 785  
 Ile Leu Asn Ile Leu Trp Cys Asp Phe Asp Lys Ser Ile Pro Leu Lys 815  
 805  
 Asn Leu Thr Phe Asn Ser Ser Ala Val Phe Thr Asp Ile Cys Ser Tyr 830  
 820  
 Pro Glu Tyr Phe Val Phe Thr Gly Val Leu Ala Met Val Thr Cys Ala 845  
 835  
 Val Phe Leu Arg Leu Asn Ser Val Leu Lys Leu Ala Val Leu Leu Ile 860  
 850  
 Met Ile Ala Ile Tyr Ala Leu Leu Thr Glu Thr Val Tyr Ala Gly Leu 880  
 865



Phe Leu Arg Tyr Asp Asn Leu Asn His Ser Gly Glu Asp Phe Leu Gly 885 890 895  
Thr Lys Glu Val Ser Leu Leu Met Ala Met Phe Leu Leu Ala Val 900 905 910  
Phe Tyr His Gly Gln Leu Gln Tyr Thr Ala Arg Leu Asp Phe Leu 915 920 925  
Trp Arg Val Gln Ala Lys Glu Glu Ile Asn Glu Met Lys Glu Leu Arg 930 935 940  
Glu His Asn Glu Asn Met Leu Arg Asn Ile Leu Pro Ser His Val Ala 945 950 955  
Arg His Phe Leu Glu Lys Asp Arg Asn Glu Glu Leu Tyr Ser Gln 965 970 975  
Ser Tyr Asp Ala Val Gly Val Met Phe Ala Ser Ile Pro Gly Phe Ala 980 985 990  
Asp Phe Tyr Ser Gln Thr Glu Met Asn Asn Gln Gly Val Glu Cys Leu 995 1000 1005  
Arg Leu Leu Asn Glu Ile Ile Ala Asp Phe Asp Glu Leu Leu Gly 1010 1015 1020  
Glu Asp Arg Phe Gln Asp Ile Glu Lys Ile Lys Thr Ile Gly Ser 1025 1030 1035  
Thr Tyr Met Ala Val Ser Gly Leu Ser Pro Glu Lys Gln Gln Cys 1040 1045 1050  
Glu Asp Lys Trp Gly His Leu Cys Ala Leu Ala Asp Phe Ser Leu 1055 1060 1065  
Ala Leu Thr Glu Ser Ile Gln Glu Ile Asn Lys His Ser Phe Asn 1070 1075 1080  
Asn Phe Glu Leu Arg Ile Gly Ile Ser His Gly Ser Val Val Ala 1085 1090 1095  
Gly Val Ile Gly Ala Lys Lys Pro Gln Tyr Asp Ile Trp Gly Lys 1100 1105 1110  
Thr Val Asn Leu Ala Ser Arg Met Asp Ser Thr Gly Val Ser Gly 1115 1120 1125  
Arg Ile Gln Val Pro Glu Glu Thr Tyr Leu Ile Leu Lys Asp Gln 1130 1135 1140  
Gly Phe Ala Phe Asp Tyr Arg Gly Glu Ile Tyr Val Lys Gly Ile 1145 1150 1155  
Ser Glu Gln Glu Gly Lys Ile Lys Thr Tyr Phe Leu Leu Gly Arg 1160 1165 1170  
Val Gln Pro Asn Pro Phe Ile Leu Pro Pro Arg Arg Leu Pro Gly 1175 1180 1185

1175 1180 1185  
Gln Tyr Ser Leu Ala Ala Val Val Leu Gly Leu Val Gln Ser Leu 1190 1195 1200  
Asn Arg Gln Arg Gln Lys Gln Leu Leu Asn Glu Asn Asn Thr 1205 1210 1215  
Gly Ile Ile Lys Gly His Tyr Asn Arg Arg Thr Leu Leu Ser Pro 1220 1225 1230  
Ser Gly Thr Glu Pro Gly Ala Gln Ala Glu Gly Thr Asp Lys Ser 1235 1240 1245  
Asp Leu Pro 1250  
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<212> PRT  
<213> Homo sapiens  
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Arg Arg Asp Gln Lys Trp His Asp Lys Lys Lys Lys Ala His Leu 20 25 30  
Gly Thr Ala Leu Lys Ala Asn Pro Phe Gly Gly Ala Ser His Ala Lys 35 40 45  
Gly Ile Val Leu Glu Lys Val Gly Val Glu Ala Lys Gln Pro Asn Ser 50 55 60  
Ala Ile Arg Lys Cys Val Arg Val Gln Leu Ile Lys Asn Gly Lys Lys 65 70 75 80  
Ile Thr Ala Phe Val Pro Asn Asp Gly Cys Leu Asn Phe Ile Glu Glu 85 90 95  
Asn Asp Glu Val Leu Val Ala Gly Phe Gly Arg Lys Gly His Ala Val 100 105 110  
Gly Asp Ile Pro Gly Val Arg Phe Lys Val Val Lys Val Ala Asn Val 115 120 125  
Ser Leu Leu Ala Leu Tyr Lys Gly Lys Lys Glu Arg Pro Arg Ser 130 135 140  
<210> 120  
<211> 144  
<212> PRT  
<213> Homo sapiens  
<400> 120  
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Thr Ala Ala Leu Ile Phe Phe Ala Ile Trp His Ile Ile Ala Phe Asp 20 25 30

Glu Leu Lys Thr Asp Tyr Lys Asn Pro Ile Asp Gln Cys Asn Thr Leu  
35 40 45

Asn Pro Leu Val Leu Pro Glu Tyr Leu Ile His Ala Phe Cys Val  
50 55 60

Met Phe Leu Cys Ala Ala Glu Trp Leu Thr Leu Gly Leu Asn Met Pro  
65 70 75 80

Leu Leu Ala Tyr His Ile Trp Arg Tyr Met Ser Arg pro Val Met Ser  
85 90 95

Gly Pro Gly Leu Tyr Asp Pro Thr Ile Met Asn Ala Asp Ile Leu  
100 105 110

Ala Tyr Cys Gln Lys Glu Gly Trp Cys Lys Leu Ala Phe Tyr Leu Leu  
115 120 125

Ala Phe Phe Tyr Tyr Leu Tyr Gly Met Ile Tyr Val Leu Val Ser Ser  
130 135 140

<210> 121  
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<213> Homo sapiens  
<400> 121

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Thr Ala Leu Trp Leu Ser Gln Leu Gly Ser Gly Thr Val Ala Ala Ser  
20 25 30

Lys Ser Val Thr Ala His Leu Ala Ala Lys Trp Pro Glu Thr Pro Leu  
35 40 45

Leu Leu Glu Ala Ser Glu Phe Met Ala Glu Glu Ser Asn Glu Lys Phe  
50 55 60

Trp Gln Phe Leu Glu Thr Val Gln Glu Leu Ala Ile Tyr Lys Gln Thr  
65 70 75 80

Glu Ser Asp Tyr Ser Tyr Tyr Asn Leu Ile Leu Lys Lys Ala Gly Gln  
85 90 95

Phe Leu Asp Asn Leu His Ile Asn Leu Leu Lys Phe Ala Phe Ser Ile  
100 105 110

Arg Ala Tyr Ser Pro Ala Ile Gln Met Phe Gln Gln Ile Ala Ala Asp  
115 120 125

Glu Pro Pro Asp Gly Cys Asn Ala Phe Val Ile His Lys Lys  
130 135 140

His Thr Cys Lys Ile Asn Glu Ile Lys Lys Leu Lys Lys Ala Ala  
145 150 155 160

Ser Arg Thr Arg Pro Tyr Leu Phe Lys Gly Asp His Lys Phe Pro Thr  
165 170 175

Asn Lys Glu Asn Leu Pro Val Val Ile Leu Tyr Ala Glu Met Gly Thr  
180 185 190

Arg Thr Phe Ser Ala Phe His Lys Val Leu Ser Glu Lys Ala Gln Asn  
195 200 205

Glu Glu Ile Leu Tyr Val Leu Arg His Tyr Ile Gln Lys Pro Ser Ser  
210 215 220

Arg Lys Met Tyr Leu Ser Gly Tyr Gly Val Glu Leu Ala Ile Lys Ser  
225 230 235 240

Thr Glu Tyr Lys Ala Leu Asp Asp Thr Gln Val Lys Thr Val Thr Asn  
245 250 255

Thr Thr Val Glu Asp Glu Thr Glu Thr Asn Glu Val Gln Gly Phe Leu  
260 265 270

Phe Gly Lys Leu Lys Glu Ile Tyr Ser Asp Leu Arg Asp Asn Leu Thr  
275 280 285

Ala Phe His Lys Tyr Leu Ile Glu Ser Asn Lys Gln Met Met Pro Leu  
290 295 300

Lys Val Trp Glu Leu Gln Asp Leu Ser Phe Gln Ala Ala Ser Gln Ile  
305 310 315 320

Met Ser Thr Pro Val Tyr Asp Ala Ile Lys Leu Met Lys Asp Ile Ser  
325 330 335

Gln Asn Phe Pro Ile Lys Ala Arg Ser Leu Thr Arg Ile Ala Val Asn  
340 345 350

Gln His Met Arg Glu Glu Ile Lys Glu Asn Gln Lys Asp Leu Gln Val  
355 360 365

Arg Phe Lys Ile Gln Pro Gly Asp Ala Arg Leu Phe Ile Asn Gly Leu  
370 375 380

Arg Val Asp Met Asp Val Tyr Asp Ala Phe Ser Ile Leu Asp Met Leu  
385 390 395 400

Lys Leu Glu Gly Lys Met Met Asn Gly Leu Arg Asn Leu Gly Ile Asn  
405 410 415

Gly Glu Asp Met Ser Lys Phe Leu Lys Leu Asn Ser His Ile Trp Glu  
420 425 430

Tyr Thr Tyr Val Leu Asp Ile Arg His Ser Ser Ile Met Trp Ile Asn  
435 440 445

Asp Leu Glu Asn Asp Asp Leu Tyr Ile Thr Trp Pro Thr Ser Cys Gln  
450 455 460

Lys Leu Leu Lys Pro Val Phe Pro Gly Ser Val Pro Ser Ile Arg Arg  
465 470 475 480

Asn Phe His Asn Leu Val Leu Phe Ile Asp Pro Ala Gln Glu Tyr Thr  
485 490 495

485 490 495  
 Leu Asp Phe Ile Lys Leu Ala Asp Val Phe Tyr Ser His Glu Val Pro  
 500 505 510  
 Leu Arg Ile Gly Phe Val Phe Ile Leu Asn Thr Asp Asp Glu Val Asp  
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 Gly Ala Asn Asp Ala Gly Val Ala Leu Trp Arg Ala Phe Asn Tyr Ile  
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 Ala Glu Glu Phe Asp Ile Ser Glu Ala Phe Ile Ser Ile Val His Met  
 545 550 555 560  
 Tyr Glu Lys Val Lys Lys Asp Glu Asn Ile Leu Thr Val Asp Asn Val  
 565 570 575  
 Lys Ser Val Leu Glu Asn Thr Phe Pro His Ala Asn Ile Trp Asp Ile  
 580 585 590  
 Leu Gly Ile His Ser Lys Tyr Asp Glu Glu Arg Lys Ala Gly Ala Ser  
 595 600 605  
 Phe Tyr Lys Met Thr Gly Leu Gly Pro Leu Pro Glu Ala Leu Tyr Asn  
 610 615 620  
 Gly Glu Pro Phe Lys His Glu Glu Met Asn Ile Lys Glu Leu Lys Met  
 625 630 635 640  
 Ala Val Leu Glu Arg Met Met Asp Ala Ser Val Tyr Leu Glu Arg Glu  
 645 650 655  
 Val Phe Leu Gly Thr Leu Asn Asp Arg Thr Asn Ala Ile Asp Phe Leu  
 660 665 670  
 Met Asp Arg Asn Asn Val Val Pro Arg Ile Asn Thr Leu Ile Leu Arg  
 675 680 685  
 Thr Asn Glu Glu Tyr Leu Asn Leu Ile Ser Thr Ser Val Thr Ala Asp  
 690 695 700  
 Val Glu Asp Phe Ser Thr Phe Phe Leu Asp Ser Glu Asn Lys Ser  
 705 710 715 720  
 Ala Val Ile Ala Lys Asn Met Tyr Tyr Leu Thr Glu Asn Asp Glu Ser  
 725 730 735  
 Ile Ile Ser Ala Val Thr Leu Trp Ile Ile Ala Asp Phe Asp Lys Pro  
 740 745 750  
 Ser Gly Arg Lys Leu Leu Phe Asn Ala Leu Lys His Met Lys Thr Ser  
 755 760 765  
 Val His Ser Arg Leu Gly Ile Ile Tyr Asn Pro Thr Ser Lys Ile Asn  
 770 775 780  
 Glu Glu Asn Thr Ala Ile Ser Arg Gly Ile Leu Ala Ala Phe Leu Thr  
 785 790 795 800

Glu Lys Asn Met Phe Leu Arg Ser Phe Leu Gly Glu Leu Ala Lys Glu  
 805 810 815  
 Glu Ile Ala Thr Thr Ile Tyr Ser Gly Asp Lys Ile Lys Thr Phe Leu  
 820 825 830  
 Ile Glu Gly Met Asp Lys Asn Ala Phe Glu Lys Lys Tyr Asn Thr Val  
 835 840 845  
 Gly Val Asn Ile Phe Arg Thr His Glu Leu Phe Cys Glu Asp Val Leu  
 850 855 860  
 Lys Leu Arg Pro Gly Glu Met Gly Ile Val Ser Asn Gly Arg Phe Leu  
 865 870 875 880  
 Gly Pro Leu Asp Glu Asp Phe Tyr Ala Glu Asp Phe Tyr Leu Leu Glu  
 885 890 895  
 Lys Ile Thr Phe Ser Asn Leu Gly Lys Ile Lys Gly Ile Val Glu  
 900 905 910  
 Asn Met Gly Ile Asn Ala Asn Asn Met Ser Asp Phe Ile Met Lys Val  
 915 920 925  
 Asp Ala Leu Met Ser Ser Val Pro Lys Arg Ala Ser Arg Tyr Asp Val  
 930 935 940  
 Thr Phe Leu Arg Glu Asn His Ser Val Ile Lys Thr Asn Pro Glu Glu  
 945 950 955 960  
 Asn Asp Met Phe Phe Asn Val Ile Ala Ile Val Asp Leu Leu Ala Arg  
 965 970 975  
 Glu Ala Glu Lys Met Ala Glu Leu Leu Val Val Leu Gly Lys Ile Ile  
 980 985 990  
 Asn Leu Lys Ile Lys Leu Phe Met Asn Cys Arg Gly Arg Leu Ser Glu  
 995 1000 1005  
 Ala Pro Leu Glu Ser Phe Tyr Arg Phe Val Leu Glu Pro Glu Leu  
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 Met Ser Gly Ala Asn Asp Val Ser Ser Leu Gly Pro Val Ala Lys  
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 Phe Leu Asp Ile Pro Glu Ser Pro Leu Leu Ile Leu Asn Met Ile  
 1040 1045 1050  
 Thr Pro Glu Gly Trp Leu Val Glu Thr Val His Ser Asn Cys Asp  
 1055 1060 1065  
 Leu Asp Asn Ile His Leu Lys Asp Thr Glu Lys Thr Ala Thr Ala  
 1070 1075 1080  
 Gly Tyr Glu Leu Glu Tyr Leu Leu Leu Glu Gly Glu Cys Phe Asp  
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 Lys Val Thr Glu Glu Pro Pro Arg Gly Leu Glu Phe Thr Leu Gly  
 1100 1105 1110

Thr Lys Asn Lys Pro Ala Val Val Asp Thr Ile Val Met Ala His  
1115 1120 1125  
His Gly Tyr Phe Gln Leu Lys Ala Asn Pro Gly Ala Trp Ile Leu  
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Arg Leu His Gln Gly Lys Ser Glu Asp Ile Tyr Gln Ile Val Gly  
1145 1150 1155  
His Glu Gly Thr Asp Ser Gln Ala Asp Leu Glu Asp Ile Ile Val  
1160 1165 1170  
Val Leu Asn Ser Phe Lys Ser Lys Ile Leu Lys Val Lys Val Lys  
1175 1180 1185  
Lys Glu Thr Asp Lys Ile Lys Glu Asp Ile Leu Thr Asp Glu Asp  
1190 1195 1200  
Glu Lys Thr Lys Gly Leu Trp Asp Ser Ile Lys Ser Phe Thr Val  
1205 1210 1215  
Ser Leu His Lys Glu Asn Lys Lys Glu Lys Asp Val Leu Asn Ile  
1220 1225 1230  
Phe Ser Val Ala Ser Gly His Leu Tyr Glu Arg Phe Leu Arg Ile  
1235 1240 1245  
Met Met Leu Ser Val Leu Arg Asn Thr Lys Thr Pro Val Lys Phe  
1250 1255 1260  
Trp Leu Leu Lys Asn Tyr Leu Ser Pro Thr Phe Lys Glu Val Ile  
1265 1270 1275  
Pro His Met Ala Lys Glu Tyr Gly Phe Arg Tyr Glu Leu Val Gln  
1280 1285 1290  
Tyr Arg Trp Pro Arg Trp Leu Arg Gln Gln Thr Glu Arg Gln Arg  
1295 1300 1305  
Ile Ile Trp Gly Tyr Lys Ile Leu Phe Leu Asp Val Leu Phe Pro  
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Leu Ala Val Asp Lys Ile Ile Phe Val Asp Ala Asp Gln Ile Val  
1325 1330 1335  
Arg His Asp Leu Lys Glu Leu Arg Asp Phe Asp Leu Asp Gly Ala  
1340 1345 1350  
Pro Tyr Gly Tyr Thr Pro Phe Cys Asp Ser Arg Glu Met Asp  
1355 1360 1365  
Gly Tyr Arg Phe Trp Lys Thr Gly Tyr Trp Ala Ser His Leu Leu  
1370 1375 1380  
Arg Arg Lys Tyr His Ile Ser Ala Leu Tyr Val Asp Leu Lys  
1385 1390 1395  
Lys Phe Arg Arg Ile Gly Ala Gly Asp Arg Leu Arg Ser Gln Tyr  
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Gln Ala Leu Ser Gln Asp Pro Asn Ser Leu Ser Asn Leu Asp Gln  
1415 1420 1425  
Asp Leu Pro Asn Asn Met Ile Tyr Gln Val Ala Ile Lys Ser Leu  
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Pro Gln Asp Trp Leu Trp Cys Glu Thr Trp Cys Asp Asp Glu Ser  
1445 1450 1455  
Lys Gln Arg Ala Lys Thr Ile Asp Leu Cys Asn Asn Pro Lys Thr  
1460 1465 1470  
Lys Glu Ser Lys Leu Lys Ala Ala Ala Arg Ile Val Pro Glu Trp  
1475 1480 1485  
Val Glu Tyr Asp Ala Glu Ile Arg Gln Leu Leu Asp His Leu Glu  
1490 1495 1500  
Asn Lys Lys Gln Asp Thr Ile Leu Thr His Asp Glu Leu  
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Cys Val Phe Ala Gln Thr Asp Glu Asn Arg Cys Leu Lys Ala Asn Ala  
20 25 30  
Lys Ser Cys Gly Glu Cys Ile Gln Ala Gly Pro Asn Cys Gly Trp Cys  
35 40 45  
Thr Asn Ser Thr Phe Leu Gln Glu Gly Met Pro Thr Ser Ala Arg Cys  
50 55 60  
Asp Asp Leu Glu Ala Leu Lys Lys Lys Gly Cys Pro Pro Asp Asp Ile  
65 70 75 80  
Glu Asn Pro Arg Gly Ser Lys Asp Ile Lys Lys Asn Lys Asn Val Thr  
85 90 95  
Asn Arg Ser Lys Gly Thr Ala Glu Lys Leu Lys Pro Glu Asp Ile His  
100 105 110  
Gln Ile Gln Pro Gln Gln Leu Val Leu Arg Leu Arg Ser Gly Glu Pro  
115 120 125  
Gln Thr Phe Thr Leu Lys Phe Lys Arg Ala Glu Asp Tyr Pro Ile Asp  
130 135 140  
Leu Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp Asp Leu Glu  
145 150 155  
Asn Val Lys Ser Leu Gly Thr Asp Leu Met Asn Glu Met Arg Arg Ile  
160 165 170 175

Thr Ser Asp Phe Arg Ile Gly Phe Gly Ser Phe Val Glu Lys Thr Val  
180 185 190

Met Pro Tyr Ile Ser Thr Thr Pro Ala Lys Leu Arg Asn Pro Cys Thr  
195 200 205

Ser Glu Gln Asn Cys Thr Thr Pro Phe Ser Tyr Lys Asn Val Leu Ser  
210 215 220

Leu Thr Asn Lys Gly Glu Val Phe Asn Glu Leu Val Gly Lys Gln Arg  
225 230 235 240

Ile Ser Gly Asn Leu Asp Ser Pro Glu Gly Gly Phe Asp Ala Ile Met  
245 250 255

Gln Val Ala Val Cys Gly Ser Leu Ile Gly Trp Arg Asn Val Thr Arg  
260 265 270

Leu Leu Val Phe Ser Thr Asp Ala Gly Phe His Phe Ala Gly Asp Gly  
275 280 285

Lys Leu Gly Gly Ile Val Leu Pro Asn Asp Gly Gln Cys His Leu Glu  
290 295 300

Asn Asn Met Tyr Thr Met Ser His Tyr Tyr Asp Tyr Pro Ser Ile Ala  
305 310 315 320

His Leu Val Gln Lys Leu Ser Glu Asn Asn Ile Gln Thr Ile Phe Ala  
325 330 335

Val Thr Glu Glu Phe Gln Pro Val Tyr Lys Glu Leu Lys Asn Leu Ile  
340 345 350

Pro Lys Ser Ala Val Gly Thr Leu Ser Ala Asn Ser Ser Asn Val Ile  
355 360 365

Gln Leu Ile Ile Asp Ala Tyr Asn Ser Leu Ser Ser Glu Val Ile Leu  
370 375 380

Glu Asn Gly Lys Leu Ser Glu Gly Val Thr Ile Ser Tyr Lys Ser Tyr  
385 390 395 400

Cys Lys Asn Gly Val Asn Gly Thr Gly Glu Asn Gly Arg Lys Cys Ser  
405 410 415

Asn Ile Ser Ile Gly Asp Glu Val Gln Phe Glu Ile Ser Ile Thr Ser  
420 425 430

Asn Lys Cys Pro Lys Lys Asp Ser Asp Ser Phe Lys Ile Arg Pro Leu  
435 440 445

Gly Phe Thr Glu Glu Val Glu Val Ile Leu Gln Tyr Ile Cys Glu Cys  
450 455 460

Glu Cys Gln Ser Glu Gly Ile Pro Glu Ser Pro Lys Cys His Glu Gly  
465 470 475 480

Asn Gly Thr Phe Glu Cys Gly Ala Cys Arg Cys Asn Glu Gly Arg Val  
485 490 495

485 490 495

Gly Arg His Cys Glu Cys Ser Thr Asp Glu Val Asn Ser Glu Asp Met  
500 505 510

Asp Ala Tyr Cys Arg Lys Glu Asn Ser Ser Glu Ile Cys Ser Asn Asn  
515 520 525

Gly Glu Cys Val Cys Gly Gln Cys Val Cys Arg Lys Arg Asp Asn Thr  
530 535 540

Asn Glu Ile Tyr Ser Gly Lys Phe Cys Glu Cys Asn Phe Asn Cys  
545 550 555 560

Asp Arg Ser Asn Gly Leu Ile Cys Gly Gly Asn Gly Val Cys Lys Cys  
565 570 575

Arg Val Cys Glu Cys Asn Pro Asn Tyr Thr Gly Ser Ala Cys Asp Cys  
580 585 590

Ser Leu Asp Thr Ser Thr Cys Glu Ala Ser Asn Gly Gln Ile Cys Asn  
595 600 605

Gly Arg Gly Ile Cys Glu Cys Gly Val Cys Lys Cys Thr Asp Pro Lys  
610 615 620

Phe Gln Gly Gln Thr Cys Glu Met Cys Gln Thr Cys Leu Gly Val Cys  
625 630 635 640

Ala Glu His Lys Glu Cys Val Gln Cys Arg Ala Phe Asn Lys Gly Glu  
645 650 655

Lys Lys Asp Thr Cys Thr Gln Glu Cys Ser Tyr Phe Asn Ile Thr Lys  
660 665 670

Val Glu Ser Arg Asp Lys Leu Pro Gln Pro Val Gln Pro Asp Pro Val  
675 680 685

Ser His Cys Lys Glu Lys Asp Val Asp Asp Cys Trp Phe Tyr Phe Thr  
690 695 700

Tyr Ser Val Asn Gly Asn Asn Glu Val Met Val His Val Val Glu Asn  
705 710 715 720

Pro Glu Cys Pro Thr Gly Pro Asp Ile Ile Pro Ile Val Ala Gly Val  
725 730 735

Val Ala Gly Ile Val Leu Ile Gly Leu Ala Leu Leu Leu Ile Trp Lys  
740 745 750

Leu Leu Met Ile Ile His Asp Arg Arg Glu Phe Ala Lys Phe Glu Lys  
755 760 765

Glu Lys Met Asn Ala Lys Trp Asp Thr Gly Glu Asn Pro Ile Tyr Lys  
770 775 780

Ser Ala Val Thr Thr Val Val Asn Pro Lys Tyr Glu Gly Lys  
785 790 795

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<213> Homo sapiens  
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Tyr Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro Asp Met Ile Leu  
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Ser Ala Ser Arg Asp Lys Thr Ile Met Trp Lys Leu Thr Arg Asp  
35 40 45  
Glu Thr Asn Tyr Gly Ile Pro Gln Arg Ala Leu Arg Gly His Ser His  
50 55 60  
Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln Phe Ala Leu Ser  
65 70 75 80  
Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp Leu Thr Thr Gly Thr  
85 90 95  
Thr Thr Arg Arg Phe Val Gly His Thr Lys Asp Val Leu Ser Val Ala  
100 105 110  
Phe Ser Ser Asp Asn Arg Gln Ile Val Ser Gly Ser Arg Asp Lys Thr  
115 120 125  
Ile Lys Leu Trp Asn Thr Leu Gly Val Cys Lys Tyr Thr Val Gln Asp  
130 135 140  
Glu Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser  
145 150 155 160  
Ser Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val  
165 170 175  
Trp Asn Leu Ala Asn Cys Lys Leu Lys Thr Asn His Ile Gly His Thr  
180 185 190  
Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala  
195 200 205  
Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly  
210 215 220  
Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys  
225 230 235  
Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile  
240 245 250  
Lys Ile Trp Asp Leu Glu Gly Lys Ile Ile Val Asp Glu Leu Lys Gln  
255 260 265 270  
Glu Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser  
275 280 285 290

Leu Ala Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp  
295 300  
Asn Leu Val Arg Val Trp Gln Val Thr Ile Gly Thr Arg  
305 310 315  
<210> 124  
<211> 351  
<212> PRT  
<213> Homo sapiens  
<400> 124  
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Ala Ser Ala Ser Val Val Lys Ala Leu Cys Ala Ala Val Leu Phe  
20 25 30  
Leu Tyr Leu Leu Ser Phe Ala Val Asp Thr Gly Cys Leu Ala Val Thr  
35 40 45  
Pro Gly Tyr Leu Phe Pro Pro Asn Phe Trp Ile Trp Thr Leu Ala Thr  
50 55 60  
His Gly Leu Met Glu Gln His Val Trp Asp Val Ala Ile Ser Leu Thr  
65 70 75 80  
Thr Val Val Val Ala Gly Arg Leu Leu Glu Pro Leu Trp Gly Ala Leu  
85 90 95  
Glu Leu Leu Ile Phe Phe Ser Val Val Asn Val Ser Val Gly Leu Leu  
100 105 110  
Gly Ala Phe Ala Tyr Leu Leu Thr Tyr Met Ala Ser Phe Asn Leu Val  
115 120 125  
Tyr Leu Phe Thr Val Arg Ile His Gly Ala Leu Gly Phe Leu Gly Gly  
130 135 140  
Val Leu Val Ala Leu Lys Gln Thr Met Gly Asp Cys Val Val Leu Arg  
145 150 155 160  
Val Pro Gln Val Arg Val Ser Val Met Pro Met Leu Leu Ala Leu  
165 170 175  
Leu Leu Leu Leu Arg Leu Ala Thr Leu Leu Gln Ser Pro Ala Leu Ala  
180 185 190  
Ser Tyr Gly Phe Gly Leu Leu Ser Ser Trp Val Tyr Leu Arg Phe Tyr  
195 200 205  
Gln Arg His Ser Arg Gly Arg Gly Asp Met Ala Asp His Phe Ala Phe  
210 215 220  
Ala Thr Phe Phe Pro Glu Ile Leu Gln Pro Val Val Gly Leu Leu Ala  
225 230 235 240  
Asn Leu Val His Ser Leu Leu Val Lys Val Lys Ile Cys Gln Lys Thr  
245 250 255

Val Lys Arg Tyr Asp Val Gly Ala Pro Ser Ser Ile Thr Ile Ser Leu  
260 265  
Pro Gly Thr Asp Pro Gln Asp Ala Glu Arg Arg Gln Leu Ala Leu  
275 280 285  
Lys Ala Leu Asn Glu Arg Leu Lys Arg Val Glu Asp Gln Ser Ile Trp  
290 295 300  
Pro Ser Met Asp Asp Glu Glu Glu Ser Gly Ala Lys Val Asp Ser  
305 310 315  
Pro Leu Pro Ser Asp Lys Ala Pro Thr Pro Pro Gly Lys Gly Ala Ala  
320 325 330 335  
Pro Glu Ser Ser Leu Ile Thr Phe Glu Ala Ala Pro Pro Thr Leu  
340 345 350  
<210> 125  
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<212> PRT  
<213> Homo sapiens  
<400> 125  
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20 25 30  
Asp Gln Asp Gly Ser Gly Asp Asp Ser Asp Asn Phe Ser Gly Ser Gly  
35 40 45  
Ala Gly Ala Leu Gln Asp Ile Thr Leu Ser Gln Gln Thr Pro Ser Thr  
50 55 60  
Trp Lys Asp Thr Gln Leu Leu Thr Ala Ile Pro Thr Ser Pro Glu Pro  
65 70 75 80  
Thr Gly Leu Glu Ala Thr Ala Ala Ser Thr Thr Leu Pro Ala Gly  
85 90 95  
Glu Gly Pro Lys Glu Gly Glu Ala Val Val Leu Pro Glu Val Glu Pro  
100 105 110  
Gly Leu Thr Ala Arg Glu Gln Glu Ala Thr Pro Arg Pro Arg Glu Thr  
115 120 125  
Thr Gln Leu Pro Thr Thr His Gln Ala Ser Thr Thr Thr Ala Thr Thr  
130 135 140  
Ala Gln Glu Pro Ala Thr Ser His Pro His Arg Asp Met Gln Pro Gly  
145 150 155 160  
His His Glu Thr Ser Thr Pro Ala Gly Pro Ser Gln Ala Asp Leu His  
165 170 175  
Thr Pro His Thr Glu Asp Gly Pro Ser Ala Thr Glu Arg Ala Ala  
180 185 190

Glu Asp Gly Ala Ser Ser Gln Leu Pro Ala Ala Glu Gly Ser Gly Glu  
195 200 205  
Gln Asp Phe Thr Phe Glu Thr Ser Gly Glu Asn Thr Ala Val Val Ala  
210 215 220  
Val Glu Pro Asp Arg Arg Asn Gln Ser Pro Val Asp Gln Gly Ala Thr  
225 230 235 240  
Gly Ala Ser Gln Gly Leu Leu Asp Arg Lys Glu Val Leu Gly Gly Val  
245 250 255  
Ile Ala Gly Gly Leu Val Gly Leu Ile Phe Ala Val Cys Leu Val Gly  
260 265 270  
Phe Met Leu Tyr Arg Met Lys Lys Asp Glu Gly Ser Tyr Ser Leu  
275 280 285  
Glu Glu Pro Lys Gln Ala Asn Gly Gly Ala Tyr Gln Lys Pro Thr Lys  
290 295 300  
Gln Glu Glu Phe Tyr Ala  
305 310  
<210> 126  
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Cys Asn Leu Phe Cys Leu Ala Asp Leu Thr Gly Ile Lys Trp Lys Lys  
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Tyr Val Trp Gln Gly Pro Thr Ser Ala Pro Ile Leu Phe Pro Val Thr  
35 40 45  
Glu Glu Asp Pro Ile Leu Ser Ser Phe Ser Arg Cys Leu Lys Ala Asp  
50 55 60  
Val Leu Gly Val Trp Arg Arg Asp Gln Arg Pro Gly Arg Arg Glu Leu  
65 70 75 80  
Trp Ile Phe Trp Trp Gly Glu Asp Pro Val Leu Leu Thr Leu Phe Thr  
85 90 95  
Met Thr Tyr Gln Lys Lys Lys Met Glu Cys Gly Arg Met Asp Phe Pro  
100 105 110  
Met Asn Ala Val Leu Cys Phe Ser Lys Ala Val His Asn Leu Leu Glu  
115 120 125  
Arg Cys Leu Met Asn Arg Asn Phe Val Arg Ile Gly Lys Trp Phe Val  
130 135 140  
Lys Pro Tyr Glu Lys Asp Glu Lys Pro Ile Asn Lys Ser Glu His Leu  
145 150 155 160

Ser Cys Ser Phe Thr Phe Leu His Gly Asp Ser Asn Val Cys Thr  
165 170 175  
Ser Val Glu Ile Asn Gln His Gln Pro Val Tyr Leu Leu Ser Glu Glu  
180 185 190  
His Ile Thr Leu Ala Gln Ser Asn Ser Pro Phe Gln Val Ile Leu  
195 200 205  
Cys Pro Phe Gly Leu Asn Gly Thr Leu Thr Gly Gln Ala Phe Lys Met  
210 215 220  
Ser Asp Ser Ala Thr Lys Lys Leu Ile Gly Glu Trp Lys Gln Phe Tyr  
225 230 235 240  
Pro Ile Ser Cys Cys Leu Lys Glu Met Ser Glu Glu Lys Gln Glu Asp  
245 250 255  
Met Asp Trp Glu Asp Asp Ser Leu Ala Ala Val Glu Val Leu Val Ala  
260 265 270  
Gly Val Arg Met Ile Tyr Pro Ala Cys Phe Val Leu Val Pro Gln Ser  
275 280 285  
Asp Ile Pro Thr Pro Ser Pro Val Gly Ser Thr His Cys Ser Ser Ser  
290 295 300  
Cys Leu Gly Val His Gln Val Pro Ala Ser Thr Arg Asp Pro Ala Met  
305 310 315 320  
Ser Ser Val Thr Leu Thr Pro Pro Thr Ser Pro Glu Glu Val Gln Thr  
325 330 335  
Val Asp Pro Gln Ser Val Gln Lys Trp Val Lys Phe Ser Ser Val Ser  
340 345 350  
Asp Gly Phe Asn Ser Asp Ser Thr Ser His His Gly Gly Lys Ile Pro  
355 360 365  
Arg Lys Leu Ala Asn His Val Val Asp Arg Val Trp Gln Glu Cys Asn  
370 375 380  
Met Asn Arg Ala Gln Asn Lys Lys Lys Tyr Ser Ala Ser Ser Gly Gly  
385 390 395 400  
Leu Cys Glu Glu Ala Thr Ala Ala Lys Val Ala Ser Trp Asp Phe Val  
405 410 415  
Glu Ala Thr Gln Arg Thr Asn Cys Ser Cys Leu Arg His Lys Asn Leu  
420 425 430  
Lys Ser Arg Asn Ala Gly Gln Gln Glu Ala Pro Ser Leu Gly Gln  
435 440 445  
Gln Gln Ile Leu Pro Lys His Lys Thr Asn Glu Lys Gln Glu Lys  
450 455 460  
Ser Glu Glu Pro Gln Lys Arg Pro Leu Thr Pro Phe His His Arg Val  
465 470 475 480

Ser Val Ser Asp Asp Val Gly Met Asp Ala Asp Ser Ala Ser Gln Arg  
485 490 495  
Leu Val Ile Ser Ala Pro Asp Ser Gln Val Arg Phe Ser Asn Ile Arg  
500 505 510  
Thr Asn Asp Val Ala Lys Thr Pro Gln Met His Gly Thr Glu Met Ala  
515 520 525  
Asn Ser Pro Gln Pro Pro Leu Ser Pro His Pro Cys Asp Val Val  
530 535 540  
Asp Glu Gly Val Thr Lys Thr Pro Ser Thr Pro Gln Ser Gln His Phe  
545 550 555 560  
Tyr Gln Met Pro Thr Pro Asp Pro Leu Val Pro Ser Lys Pro Met Glu  
565 570 575  
Asp Arg Ile Asp Ser Leu Ser Gln Ser Phe Pro Pro Gln Tyr Gln Glu  
580 585 590  
Ala Val Glu Pro Thr Val Tyr Val Gly Thr Ala Val Asn Leu Glu Glu  
595 600 605  
Asp Glu Ala Asn Ile Ala Trp Lys Tyr Tyr Lys Phe Pro Lys Lys Lys  
610 615 620  
Asp Val Glu Phe Leu Pro Pro Gln Leu Pro Ser Asp Lys Phe Lys Asp  
625 630 635  
Asp Pro Val Gly Pro Phe Gly Gln Glu Ser Val Thr Ser Val Thr Glu  
640 645 650 655  
Leu Met Val Gln Cys Lys Lys Pro Leu Lys Val Ser Asp Glu Leu Val  
660 665 670  
Gln Gln Tyr Gln Ile Lys Asn Gln Cys Leu Ser Ala Ile Ala Ser Asp  
675 680 685  
Ala Glu Gln Glu Pro Lys Ile Asp Pro Tyr Ala Phe Val Glu Gly Asp  
690 695 700  
Glu Glu Phe Leu Phe Pro Asp Lys Lys Asp Arg Gln Asn Ser Glu Arg  
705 710 715 720  
Glu Ala Gly Lys Lys His Lys Val Glu Asp Gly Thr Ser Ser Val Thr  
725 730 735  
Val Leu Ser His Glu Glu Asp Ala Met Ser Leu Phe Ser Pro Ser Ile  
740 745 750  
Lys Gln Asp Ala Pro Arg Pro Thr Ser His Ala Arg Pro Pro Ser Thr  
755 760 765  
Ser Leu Ile Tyr Asp Ser Asp Leu Ala Val Ser Tyr Thr Asp Leu Asp  
770 775 780  
Asn Leu Phe Asn Ser Asp Glu Asp Glu Leu Thr Pro Gly Ser Lys Arg  
785 790 795 800



Ser Ala Asn Gly Ser Asp Asp Lys Ala Ser Cys Lys Glu Ser Lys Thr  
805 810 815

Gly Asn Leu Asp Pro Leu Ser Cys Ile Ser Thr Ala Asp Leu His Lys  
820 825 830

Met Tyr Pro Thr Pro Ser Leu Glu Glu His Ile Met Gly Phe Ser  
835 840 845

Pro Met Asn Met Asn Asn Lys Glu Tyr Gly Ser Met Asp Thr Thr Pro  
850 855 860

Gly Gly Thr Val Leu Glu Gly Asn Ser Ser Ser Ile Gly Ala Glu Phe  
865 870 875 880

Lys Ile Glu Val Asp Glu Gly Phe Cys Ser Pro Lys Pro Ser Glu Ile  
885 890 895

Lys Asp Phe Ser Tyr Val Tyr Lys Pro Glu Asn Cys Glu Ile Leu Val  
900 905 910

Gly Cys Ser Met Phe Ala Pro Leu Lys Thr Leu Pro Ser Glu Tyr Leu  
915 920 925

Pro Leu Ile Lys Leu Pro Glu Glu Cys Ile Tyr Arg Glu Ser Trp Thr  
930 935 940

Val Gly Lys Leu Glu Leu Ser Ser Gly Pro Ser Met Pro Phe Ile  
945 950 955 960

Lys Glu Gly Asp Gly Ser Asn Met Asp Glu Glu Tyr Gly Thr Ala Tyr  
965 970 975

Thr Pro Glu Thr His Thr Ser Cys Gly Met Pro Pro Ser Ser Ala Pro  
980 985 990

Pro Ser Asn Ser Gly Ala Gly Ile Leu Pro Ser Pro Ser Thr Pro Arg  
995 1000 1005

Phe Pro Thr Pro Arg Thr Pro Arg Thr Pro Arg Gly  
1010 1015 1020

Ala Gly Gly Pro Ala Ser Ala Glu Gly Ser Val Lys Tyr Glu Asn  
1025 1030 1035

Ser Asp Leu Tyr Ser Pro Ala Ser Thr Pro Ser Thr Cys Arg Pro  
1040 1045 1050

Leu Asn Ser Val Glu Pro Ala Thr Val Pro Ser Ile Pro Glu Ala  
1055 1060 1065

His Ser Leu Tyr Val Asn Leu Ile Leu Ser Glu Ser Val Met Asn  
1070 1075 1080

Leu Phe Lys Asp Cys Asn Ser Asp Ser Cys Cys Ile Cys Val Cys  
1085 1090 1095

Asn Met Asn Ile Lys Gly Ala Asp Val Gly Val Tyr Ile Pro Asp

1100 1105 1110

Pro Thr Glu Glu Ala Glu Tyr Arg Cys Thr Cys Gly Phe Ser Ala  
1115 1120 1125

Val Met Asn Arg Lys Phe Gly Asn Asn Ser Gly Leu Phe Leu Glu  
1130 1135 1140

Asp Glu Leu Asp Ile Ile Gly Arg Asn Thr Asp Cys Gly Lys Glu  
1145 1150 1155

Ala Glu Lys Arg Phe Glu Ala Leu Arg Ala Thr Ser Ala Glu His  
1160 1165 1170

Val Asn Gly Gly Leu Lys Glu Ser Glu Lys Leu Ser Asp Asp Leu  
1175 1180 1185

Ile Leu Leu Leu Glu Asn Asp Glu Cys Thr Asn Leu Phe Ser Pro Phe  
1190 1195 1200

Gly Ala Ala Asp Glu Asn Pro Phe Pro Lys Ser Gly Val Ile Ser  
1205 1210 1215

Asn Trp Val Arg Val Glu Glu Arg Asp Cys Asn Asp Cys Tyr  
1220 1225 1230

Leu Ala Leu Glu His Gly Arg Glu Phe Met Asp Asn Met Ser Gly  
1235 1240 1245

Gly Lys Val Asp Glu Ala Leu Val Lys Ser Ser Cys Leu His Pro  
1250 1255 1260

Trp Ser Lys Arg Asn Asp Val Ser Met Glu Cys Ser Glu Asp Ile  
1265 1270 1275

Leu Arg Met Leu Leu Ser Leu Glu Pro Val Leu Glu Asp Ala Ile  
1280 1285 1290

Glu Lys Lys Arg Thr Val Arg Pro Trp Gly Val Glu Gly Pro Leu  
1295 1300 1305

Thr Trp Glu Glu Phe His Lys Met Ala Gly Arg Gly Ser Tyr Gly  
1310 1315 1320

Thr Asp Glu Ser Pro Glu Pro Leu Pro Ile Pro Thr Phe Leu Leu  
1325 1330 1335

Gly Tyr Asp Tyr Asp Tyr Leu Val Leu Ser Pro Phe Ala Leu Pro  
1340 1345 1350

Tyr Trp Glu Arg Leu Met Leu Glu Pro Tyr Gly Ser Glu Arg Asp  
1355 1360 1365

Ile Ala Tyr Val Val Leu Cys Pro Glu Asn Glu Ala Leu Leu Asn  
1370 1375 1380

Gly Ala Lys Ser Phe Phe Arg Asp Leu Thr Ala Ile Tyr Glu Ser  
1385 1390 1395

Cys Arg Leu Gly Gln His Arg Pro Val Ser Arg Leu Leu Thr Asp  
1400 1403 1410  
Gly Ile Met Arg Val Gly Ser Thr Ala Ser Lys Lys Leu Ser Glu  
1415 1420 1425  
Lys Leu Val Ala Glu Trp Phe Ser Gln Ala Ala Asp Gly Asn Asn  
1430 1435 1440  
Glu Ala Phe Ser Lys Leu Lys Leu Tyr Ala Gln Val Cys Arg Tyr  
1445 1450 1455  
Asp Leu Gly Pro Tyr Leu Ala Ser Leu Pro Leu Asp Ser Ser Leu  
1460 1465 1470  
Leu Ser Gln Pro Asn Leu Val Ala Pro Thr Ser Gln Ser Leu Ile  
1475 1480 1485  
Thr Pro Pro Gln Met Thr Asn Thr Gly Asn Ala Asn Thr Pro Ser  
1490 1495 1500  
Ala Thr Leu Ala Ser Ala Ala Ser Ser Thr Met Thr Val Thr Ser  
1505 1510 1515  
Gly Val Ala Ile Ser Thr Ser Val Ala Thr Ala Asn Ser Thr Leu  
1520 1525 1530  
Thr Thr Ala Ser Thr Ser Ser Ser Ser Ser Asn Leu Asn Ser  
1535 1540 1545  
Gly Val Ser Ser Asn Lys Leu Pro Ser Phe Pro Phe Gly Ser  
1550 1555 1560  
Met Asn Ser Asn Ala Ala Gly Ser Met Ser Thr Gln Ala Asn Thr  
1565 1570 1575  
Val Gln Ser Gly Gln Leu Gly Gly Gln Gln Thr Ser Ala Leu Gln  
1580 1585 1590  
Thr Ala Gly Ile Ser Gly Glu Ser Ser Ser Ser Leu Pro Thr Gln Pro  
1595 1600 1605  
His Pro Asp Val Ser Glu Ser Thr Met Asp Arg Lys Val Gly  
1610 1615 1620  
Ile Pro Thr Asp Gly Asp Ser His Ala Val Thr Tyr Pro Pro Ala  
1625 1630 1635  
Ile Val Val Tyr Ile Ile Asp Pro Phe Thr Tyr Glu Asn Thr Asp  
1640 1645 1650  
Glu Ser Thr Asn Ser Ser Ser Val Trp Thr Leu Gly Leu Leu Arg  
1655 1660 1665  
Cys Phe Leu Glu Met Val Gln Thr Leu Pro Pro His Ile Lys Ser  
1670 1675 1680  
Thr Val Ser Val Gln Ile Ile Pro Cys Gln Tyr Leu Leu Gln Pro  
1685 1690 1695

Val Lys His Glu Asp Arg Glu Ile Tyr Pro Gln His Leu Lys Ser  
1700 1705 1710  
Leu Ala Phe Ser Ala Phe Thr Gln Cys Arg Arg Pro Leu Pro Thr  
1715 1720 1725  
Ser Thr Asn Val Lys Thr Leu Thr Gly Phe Gly Pro Gly Leu Ala  
1730 1735 1740  
Met Glu Thr Ala Leu Arg Ser Pro Asp Arg Pro Glu Cys Ile Arg  
1745 1750 1755  
Leu Tyr Ala Pro Pro Phe Ile Leu Ala Pro Val Lys Asp Lys Gln  
1760 1765 1770  
Thr Glu Leu Gly Glu Thr Phe Gly Glu Ala Gly Gln Lys Tyr Asn  
1775 1780 1785  
Val Leu Phe Val Gly Tyr Cys Leu Ser His Asp Gln Arg Trp Ile  
1790 1795 1800  
Leu Ala Ser Cys Thr Asp Leu Tyr Gly Glu Leu Leu Glu Thr Cys  
1805 1810 1815  
Ile Ile Asn Ile Asp Val Pro Asn Arg Ala Arg Arg Lys Lys Ser  
1820 1825 1830  
Ser Ala Arg Lys Phe Gly Leu Gln Lys Leu Trp Glu Trp Cys Leu  
1835 1840 1845  
Gly Leu Val Gln Met Ser Ser Leu Pro Trp Arg Val Val Ile Gly  
1850 1855 1860  
Arg Leu Gly Arg Ile Gly His Gly Glu Leu Lys Asp Trp Ser Cys  
1865 1870 1875  
Leu Leu Ser Arg Arg Asn Leu Gln Ser Leu Ser Lys Arg Leu Lys  
1880 1885 1890  
Asp Met Cys Arg Met Cys Gly Ile Ser Ala Ala Asp Ser Pro Ser  
1895 1900 1905  
Ile Leu Ser Ala Cys Leu Val Ala Met Glu Pro Gln Gly Ser Phe  
1910 1915 1920  
Val Ile Met Pro Asp Ser Val Ser Thr Gly Ser Val Phe Gly Arg  
1925 1930 1935  
Ser Thr Thr Leu Asn Met Gln Thr Ser Gln Leu Asn Thr Pro Gln  
1940 1945 1950  
Asp Thr Ser Cys Thr His Ile Leu Val Phe Pro Thr Ser Ala Ser  
1955 1960 1965  
Val Gln Val Ala Ser Ala Thr Tyr Thr Thr Glu Asn Leu Asp Leu  
1970 1975 1980  
Ala Phe Asn Pro Asn Asn Asp Gly Ala Asp Gly Met Gly Ile Phe  
1985 1990 1995

Asp Leu Leu Asp Thr Gly Asp Asp Leu Asp Pro Asp Ile Ile Asn  
2000 2005 2010  
Ile Leu Pro Ala Ser Pro Thr Gly Ser Pro Val His Ser Pro Gly  
2015 2020 2025  
Ser His Tyr Pro His Gly Gly Asp Ala Gly Lys Gly Gln Ser Thr  
2030 2035 2040  
Asp Arg Leu Leu Ser Thr Glu Pro His Glu Glu Val Pro Asn Ile  
2045 2050 2055  
Leu Gln Gln Pro Leu Ala Leu Gly Tyr Phe Val Ser Thr Ala Lys  
2060 2065 2070  
Ala Gly Pro Leu Pro Asp Trp Phe Trp Ser Ala Cys Pro Gln Ala  
2075 2080 2085  
Gln Tyr Gln Cys Pro Leu Phe Leu Lys Ala Ser Leu His Leu His  
2090 2100  
Val Pro Ser Val Gln Ser Asp Glu Leu Leu His Ser Lys His Ser  
2105 2110 2115  
His Pro Leu Asp Ser Asn Gln Thr Ser Asp Val Leu Arg Phe Val  
2120 2125 2130  
Leu Glu Gln Tyr Asn Ala Leu Ser Trp Leu Thr Cys Asp Pro Ala  
2135 2140 2145  
Thr Gln Asp Arg Ser Cys Leu Pro Ile His Phe Val Val Leu  
2150 2155 2160  
Asn Gln Leu Tyr Asn Phe Ile Met Asn Met Leu  
2165 2170  
<210> 127  
<211> 415  
<212> PRT  
<213> Homo sapiens  
<400> 127  
Met Glu Leu Arg Val Gly Asn Arg Tyr Arg Leu Gly Arg Lys Ile Gly  
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Ser Gly Ser Phe Gly Asp Ile Tyr Leu Gly Thr Asp Ile Ala Ala Gly  
20 25 30  
Glu Glu Val Ala Ile Lys Leu Glu Cys Val Lys Thr Lys His Pro Gln  
35 40 45  
Leu His Ile Glu Ser Lys Ile Tyr Lys Met Met Gln Gly Gly Val Gly  
50 55 60  
Ile Pro Thr Ile Arg Trp Cys Gly Ala Glu Gly Asp Tyr Asn Val Met  
65 70 75 80  
Val Met Glu Leu Leu Gly Pro Ser Leu Glu Asp Leu Phe Asn Phe Cys  
85 90 95

Ser Arg Lys Phe Ser Leu Lys Thr Val Leu Leu Ala Asp Gln Met  
100 105 110  
Ile Ser Arg Ile Glu Tyr Ile His Ser Lys Asn Phe Ile His Arg Asp  
115 120 125  
Val Lys Pro Asp Asn Phe Leu Met Gly Leu Gly Lys Lys Gly Asn Leu  
130 135 140  
Val Tyr Ile Ile Asp Phe Gly Leu Ala Lys Lys Tyr Arg Asp Ala Arg  
145 150 155 160  
Thr His Gln His Ile Pro Tyr Arg Glu Asn Lys Asn Leu Thr Gly Thr  
165 170 175  
Ala Arg Tyr Ala Ser Ile Asn Thr His Leu Gly Ile Glu Gln Ser Arg  
180 185 190  
Arg Asp Asp Leu Glu Ser Leu Gly Tyr Val Leu Met Tyr Phe Asn Leu  
195 200 205  
Gly Ser Leu Pro Trp Gln Gly Leu Lys Ala Thr Lys Arg Gln Lys  
210 215 220  
Tyr Glu Arg Ile Ser Glu Lys Lys Met Ser Thr Pro Ile Glu Val Leu  
225 230 235 240  
Cys Lys Gly Tyr Pro Ser Glu Phe Ala Thr Tyr Leu Asn Phe Cys Arg  
245 250 255  
Ser Leu Arg Phe Asp Lys Pro Asp Tyr Ser Tyr Leu Arg Gln Leu  
260 265 270  
Phe Arg Asn Leu Phe His Arg Gln Gly Phe Ser Tyr Asp Tyr Val Phe  
275 280 285  
Asp Trp Asn Met Leu Lys Phe Gly Ala Ser Arg Ala Ala Asp Asp Ala  
290 295 300  
Glu Arg Glu Arg Arg Asp Arg Glu Glu Arg Leu Arg His Ser Arg Asn  
305 310 315 320  
Pro Ala Thr Arg Gly Leu Pro Ser Thr Asp Ser Gly Arg Leu Arg Gly  
325 330 335  
Thr Gln Glu Val Ala Pro Pro Thr Pro Leu Thr Pro Thr Ser His Thr  
340 345 350  
Ala Asn Thr Ser Pro Arg Pro Val Ser Gly Met Glu Arg Glu Arg Lys  
355 360 365  
Val Ser Met Arg Leu His Arg Gly Ala Pro Val Asn Ile Ser Ser Ser  
370 375 380  
Asp Leu Thr Gly Arg Gln Asp Thr Ser Arg Met Ser Thr Ser Gln Ile  
385 390 395 400  
Pro Gly Arg Val Ala Ser Ser Gly Leu Gln Ser Val Val His Arg

405 410 415

<210> 128  
 <211> 204  
 <212> PRT  
 <213> Homo sapiens  
 <400> 128

Met Thr Glu Trp Glu Thr Ala Ala Pro Ala Val Ala Glu Thr Pro Asp  
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Ile Lys Leu Phe Gly Lys Trp Ser Thr Asp Asp Val Gln Ile Asn Asp  
 20 25 30

Ile Ser Leu Gln Asp Tyr Ile Ala Val Lys Glu Lys Tyr Ala Lys Tyr  
 35 40 45

Leu Pro His Ser Ala Gly Arg Tyr Ala Ala Asn Ala Phe Arg Lys Ala  
 50 55 60

Gln Cys Pro Ile Val Glu Arg Leu Thr Asn Ser Met Met Met His Gly  
 65 70 75 80

Arg Asn Asn Gly Lys Lys Leu Met Thr Val Arg Ile Val Lys His Ala  
 85 90 95

Phe Glu Ile Ile His Leu Leu Thr Gly Glu Asn Pro Leu Gln Val Leu  
 100 105 110

Val Asn Ala Ile Ile Asn Ser Gly Pro Arg Glu Asp Ser Thr Arg Ile  
 115 120 125

Gly Arg Ala Gly Thr Val Arg Arg Gln Ala Val Asp Val Ser Pro Leu  
 130 135 140

Arg Arg Val Asn Gln Ala Ile Trp Leu Leu Cys Thr Gly Ala Arg Glu  
 145 150 155 160

Ala Ala Phe Arg Asn Ile Lys Thr Ile Ala Glu Cys Leu Ala Asp Glu  
 165 170 175

Leu Ile Asn Ala Ala Lys Gly Ser Ser Asn Ser Tyr Ala Ile Lys Lys  
 180 185 190

Lys Asp Glu Leu Glu Arg Val Ala Lys Ser Asn Arg  
 195 200

<210> 129  
 <211> 694  
 <212> PRT  
 <213> Homo sapiens  
 <400> 129

Met Glu Asn Lys Ser Leu Glu Ser Ser Gln Thr Asp Leu Lys Leu Val  
 1 5 10 15

Ala His Pro Arg Ala Lys Ser Lys Val Trp Lys Tyr Phe Gly Phe Asp  
 20 25 30

Thr Asn Ala Glu Gly Cys Ile Leu Gln Trp Lys Lys Ile Tyr Cys Arg  
 35 40 45

Ile Cys Met Ala Gln Ile Ala Tyr Ser Gly Asn Thr Ser Asn Leu Ser  
 50 55 60

Tyr His Leu Glu Lys Asn His Pro Glu Glu Phe Cys Glu Phe Val Lys  
 65 70 75 80

Ser Asn Thr Glu Gln Met Arg Glu Ala Phe Ala Thr Ala Phe Ser Lys  
 85 90 95

Leu Lys Pro Glu Ser Ser Gln Gln Pro Gly Gln Asp Ala Leu Ala Val  
 100 105 110

Lys Ala Gly His Gly Tyr Asp Ser Lys Lys Gln Gln Glu Leu Thr Ala  
 115 120 125

Ala Val Leu Gly Leu Ile Cys Glu Gly Leu Tyr Pro Ala Ser Ile Val  
 130 135 140

Asp Glu Pro Thr Phe Lys Val Leu Leu Lys Thr Ala Asp Pro Arg Tyr  
 145 150 155 160

Glu Leu Pro Ser Arg Lys Tyr Ile Ser Thr Lys Ala Ile Pro Glu Lys  
 165 170 175

Tyr Gly Ala Val Arg Glu Val Ile Leu Lys Glu Leu Ala Glu Ala Thr  
 180 185 190

Trp Cys Gly Ile Ser Thr Asp Met Trp Arg Ser Glu Asn Gln Asn Arg  
 195 200 205

Ala Tyr Val Thr Leu Ala His Phe Leu Gly Leu Gly Ala Pro Asn  
 210 215 220

Cys Leu Ser Met Gly Ser Arg Cys Leu Lys Thr Phe Glu Val Pro Glu  
 225 230 235 240

Glu Asn Thr Ala Glu Thr Ile Thr Arg Val Leu Tyr Glu Val Phe Ile  
 245 250 255

Glu Trp Gly Ile Ser Ala Lys Val Phe Gly Ala Thr Thr Asn Tyr Gly  
 260 265 270

Lys Asp Ile Val Lys Ala Cys Ser Leu Leu Asp Val Ala Val His Met  
 275 280 285

Pro Cys Leu Gly His Thr Phe Asn Ala Gly Ile Gln Gln Ala Phe Gln  
 290 295 300

Leu Pro Lys Leu Gly Ala Leu Leu Ser Arg Cys Arg Lys Leu Val Glu  
 305 310 315 320

Tyr Phe Gln Gln Ser Ala Val Ala Met Tyr Met Leu Tyr Glu Lys Gln  
 325 330 335

Lys Gln Gln Asn Val Ala His Cys Met Leu Val Ser Asn Arg Val Ser  
 340 345 350

Trp Trp Gly Ser Thr Leu Ala Met Leu Gln Arg Leu Lys Glu Gln Gln  
 355 360 365

335 360 380 395 400  
Phe Val Ile Ala Gly Val Leu Val Glu Asp Ser Asn Asn His His Leu  
370 375 380 395 400  
Met Leu Glu Ala Ser Glu Trp Ala Thr Ile Glu Gly Leu Val Glu Leu  
385 390 395 400 405  
Leu Gln Pro Phe Lys Gln Val Ala Glu Met Leu Ser Ala Ser Arg Tyr  
400 405 410 415  
Pro Thr Ile Ser Met Val Lys Pro Leu Leu His Met Leu Leu Asn Thr  
420 425 430  
Thr Leu Asn Ile Lys Glu Thr Asp Ser Lys Glu Leu Ser Met Ala Lys  
435 440 445  
Glu Val Ile Ala Lys Glu Leu Ser Lys Thr Tyr Gln Glu Thr Pro Glu  
450 455 460  
Ile Asp Met Phe Leu Asn Val Ala Thr Phe Leu Asp Pro Arg Tyr Lys  
465 470 475  
Arg Leu Pro Phe Leu Ser Ala Phe Glu Arg Gln Gln Val Glu Asn Arg  
485 490 495  
Val Val Glu Glu Ala Lys Gly Leu Leu Asp Lys Val Lys Asp Gly Gly  
500 505 510  
Tyr Arg Pro Ala Glu Asp Lys Ile Phe Pro Val Pro Glu Glu Pro Pro  
515 520 525  
Val Lys Lys Leu Met Arg Thr Ser Thr Pro Pro Ala Ser Val Ile  
530 535 540  
Asn Asn Met Leu Ala Glu Ile Phe Cys Gln Thr Gly Gly Val Glu Asp  
545 550 555  
Gln Glu Glu Trp His Ala Gln Val Val Glu Glu Leu Ser Asn Phe Lys  
565 570 575  
Ser Gln Lys Val Leu Gly Leu Asn Glu Asp Pro Leu Lys Trp Trp Ser  
580 585 590  
Asp Arg Leu Ala Leu Phe Pro Leu Leu Pro Lys Val Leu Gln Lys Tyr  
595 600 605  
Trp Cys Val Thr Ala Thr Arg Val Ala Pro Glu Arg Leu Phe Gly Ser  
610 615 620  
Ala Ala Asn Val Val Ser Ala Lys Arg Asn Arg Leu Ala Pro Ala His  
625 630 635  
Val Asp Glu Gln Val Phe Leu Tyr Glu Asn Ala Arg Ser Gly Ala Glu  
645 650 655  
Ala Glu Pro Glu Asp Gln Asp Glu Gly Glu Trp Gly Leu Asp Gln Glu  
660 665 670

675 680 685  
Gln Val Phe Ser Leu Gly Asp Gly Val Ser Lys Lys Gly Lys Ile  
675 680 685  
Arg Asp Ser Ser Phe Leu  
690  
<210> 130  
<211> 729  
<212> PRT  
<213> Homo sapiens  
<400> 130  
Met Gly Lys Lys Tyr Lys Asn Ile Val Leu Leu Lys Gly Leu Glu Val  
1 5 10 15  
Ile Asn Asp Tyr His Phe Arg Met Val Lys Ser Leu Leu Ser Asn Asp  
20 25 30  
Leu Lys Leu Asn Leu Lys Met Arg Glu Glu Tyr Asp Lys Ile Gln Ile  
35 40 45  
Ala Asp Leu Met Glu Glu Lys Phe Arg Gly Asp Ala Gly Leu Gly Lys  
50 55 60  
Leu Ile Lys Ile Phe Glu Asp Ile Pro Thr Leu Glu Asp Leu Ala Glu  
65 70 75 80  
Thr Leu Lys Lys Glu Lys Leu Lys Val Lys Gly Pro Ala Leu Ser Arg  
85 90 95  
Lys Arg Lys Lys Glu Val His Ala Thr Ser Pro Ala Pro Ser Thr Ser  
100 105 110  
Ser Thr Val Lys Thr Glu Gly Ala Glu Ala Thr Pro Gly Ala Gln Lys  
115 120 125  
Arg Lys Lys Ser Thr Lys Glu Lys Ala Gly Pro Lys Gly Ser Lys Val  
130 135 140  
Ser Glu Glu Gln Thr Gln Pro Pro Ser Pro Ala Gly Ala Gly Met Ser  
145 150 155 160  
Thr Ala Met Gly Arg Ser Pro Ser Pro Lys Thr Ser Leu Ser Ala Pro  
165 170 175  
Pro Asn Ser Ser Thr Glu Asn Pro Lys Thr Val Ala Lys Cys Gln  
180 185 190  
Val Thr Pro Arg Arg Asn Val Leu Gln Lys Arg Pro Val Ile Val Lys  
195 200 205  
Val Leu Ser Thr Thr Lys Pro Phe Glu Tyr Glu Thr Pro Glu Met Glu  
210 215 220  
Lys Lys Ile Met Phe His Ala Thr Val Ala Thr Gln Thr Gln Phe Phe  
225 230 235 240  
His Val Lys Val Leu Asn Thr Ser Leu Lys Glu Lys Phe Asn Gly Lys  
245 250 255

Lys Ile Ile Ile Ser Asp Tyr Leu Glu Tyr Asp Ser Leu Leu Glu 265 270  
Val Asn Glu Glu Ser Thr Val Ser Glu Ala Gly Pro Asn Gln Thr Phe 275 285  
Glu Val Pro Asn Lys Ile Ile Asn Arg Ala Lys Glu Thr Leu Lys Ile 290 300  
Asp Ile Leu His Lys Gln Ala Ser Gly Asn Ile Val Tyr Gly Val Phe 305 315  
Met Leu His Lys Lys Thr Val Asn Gln Lys Thr Thr Ile Tyr Glu Ile 320 335  
Gln Asp Asp Arg Gly Lys Met Asp Val Val Gly Thr Gly Gln Cys His 340 350  
Asn Ile Pro Cys Glu Glu Gly Asp Lys Leu Gln Leu Phe Cys Phe Arg 355 365  
Leu Arg Lys Lys Asn Gln Met Ser Lys Leu Ile Ser Glu Met His Ser 370 380  
Phe Ile Gln Ile Lys Lys Lys Thr Asn Pro Arg Asn Asn Asp Pro Lys 385 395  
Ser Met Lys Leu Pro Gln Gln Gln Arg Gln Leu Pro Tyr Pro Ser Glu 400 415  
Ala Ser Thr Thr Phe Pro Glu Ser His Leu Arg Thr Pro Gln Met Pro 420 430  
Pro Thr Thr Pro Ser Ser Phe Phe Thr Lys Lys Ser Glu Asp Thr 435 445  
Ile Ser Lys Met Asn Asp Phe Met Arg Met Gln Ile Leu Lys Glu Gly 450 460  
Ser His Phe Pro Gly Pro Phe Met Thr Ser Ile Gly Pro Ala Glu Ser 465 475  
His Pro His Thr Pro Gln Met Pro Pro Ser Thr Pro Ser Ser Ser Phe 480 495  
Leu Thr Thr Leu Lys Pro Arg Leu Lys Thr Glu Pro Glu Glu Val Ser 500 510  
Ile Glu Asp Ser Ala Gln Ser Asp Leu Lys Glu Val Met Val Leu Asn 515 525  
Ala Thr Glu Ser Phe Val Tyr Glu Pro Lys Glu Gln Lys Lys Met Phe 530 540  
His Ala Thr Val Ala Thr Glu Asn Glu Val Phe Arg Val Lys Val Phe 545 555  
Asn Ile Asp Leu Lys Glu Lys Phe Thr Pro Lys Lys Ile Ile Ala Ile 560 575

Ala Asn Tyr Val Cys Arg Asn Gly Phe Leu Glu Val Tyr Pro Phe Thr 580 595  
Leu Val Ala Asp Val Asn Ala Asp Arg Asn Met Glu Ile Pro Lys Gly 595 605  
Leu Ile Arg Ser Ala Ser Val Thr Pro Lys Ile Asn Gln Leu Cys Ser 610 620  
Gln Thr Lys Gly Ser Phe Val Asn Gly Val Phe Glu Val His Lys Lys 625 635  
Asn Val Arg Gly Glu Phe Thr Tyr Tyr Glu Ile Gln Asp Asn Thr Gly 640 655  
Lys Met Glu Val Val Val His Gly Arg Leu Asn Thr Ile Asn Cys Glu 660 670  
Glu Gly Asp Lys Leu Lys Leu Thr Ser Phe Glu Leu Ala Pro Lys Ser 675 685  
Gly Asn Thr Gly Glu Leu Arg Ser Val Ile His Ser His Ile Lys Val 690 700  
Ile Lys Thr Arg Lys Asn Lys Lys Asp Ile Leu Asn Pro Asp Ser Ser 705 715  
Met Glu Thr Ser Pro Asp Phe Phe 720 725  
<210> 131  
<211> 216  
<212> PRT  
<213> Homo sapiens  
<400> 131  
Met Leu Arg Leu Ser Glu Arg Asn Met Lys Val Leu Leu Ala Ala 1 15  
Leu Ile Ala Gly Ser Val Phe Phe Leu Leu Leu Pro Gly Pro Ser Ala 20 30  
Ala Asp Glu Lys Lys Lys Gly Pro Lys Val Thr Val Lys Val Tyr Phe 35 45  
Asp Leu Arg Ile Gly Asp Glu Asp Val Gly Arg Val Ile Phe Gly Leu 50 60  
Phe Gly Lys Thr Val Pro Lys Thr Val Asp Asn Phe Val Ala Leu Ala 65 80  
Thr Gly Glu Lys Gly Phe Gly Tyr Lys Asn Ser Lys Phe His Arg Val 85 95  
Ile Lys Asp Phe Met Ile Gln Gly Gly Asp Phe Thr Arg Gly Asp Gly 100 110  
Thr Gly Gly Lys Ser Ile Tyr Gly Glu Arg Phe Pro Asp Glu Asn Phe 115 125

Lys Leu Lys His Tyr Gly Pro Gly Trp Val Ser Met Ala Asn Ala Gly  
130 135 140

Lys Asp Thr Asn Gly Ser Gln Phe Ile Thr Thr Val Lys Thr Ala  
145 150 155

Trp Leu Asp Gly Lys His Val Val Phe Gly Lys Val Leu Gly Met  
165 170 175

Glu Val Val Arg Lys Val Glu Ser Thr Thr Lys Thr Asp Ser Arg Asp Lys  
180 185 190

Pro Leu Lys Asp Val Ile Ile Ala Asp Cys Gly Lys Ile Glu Val Glu  
195 200 205

Lys Pro Phe Ala Ile Ala Lys Glu  
210 215

<210> 132

<211> 208

<212> PRT

<213> Homo sapiens

<400> 132

Met Lys Leu Leu Pro Ser Val Val Leu Lys Leu Phe Leu Ala Ala Val  
1 5 10 15

Leu Ser Ala Leu Val Thr Gly Glu Ser Leu Glu Arg Leu Arg Gly  
20 25 30

Leu Ala Ala Gly Thr Ser Asn Pro Asp Pro Thr Val Ser Thr Asp  
35 40 45

Gln Leu Leu Pro Leu Gly Gly Gly Arg Asp Arg Lys Val Arg Asp Leu  
50 55 60

Gln Glu Ala Asp Leu Asp Leu Leu Arg Val Thr Leu Ser Ser Lys Pro  
65 70 75 80

Gln Ala Leu Ala Thr Pro Asn Lys Glu Glu His Gly Lys Arg Lys Lys  
85 90 95

Lys Gly Lys Gly Leu Gly Lys Lys Arg Asp Pro Cys Leu Arg Lys Tyr  
100 105 110

Lys Asp Phe Cys Ile His Gly Glu Cys Lys Tyr Val Lys Glu Leu Arg  
115 120 125

Ala Pro Ser Cys Ile Cys His Pro Gly Tyr His Gly Glu Arg Cys His  
130 135 140

Gly Leu Ser Leu Pro Val Glu Asn Arg Leu Tyr Thr Tyr Asp His Thr  
145 150 155 160

Thr Ile Leu Ala Val Val Ala Val Val Leu Ser Ser Val Cys Leu Leu  
165 170 175

Val Ile Val Gly Leu Leu Met Phe Arg Tyr His Arg Arg Gly Tyr  
180 185 190

Asp Val Glu Asn Glu Glu Lys Val Lys Leu Gly Met Thr Asn Ser His  
195 200 205

<210> 133

<211> 178

<212> PRT

<213> Homo sapiens

<400> 133

Met Thr Thr Leu Arg Ala Phe Thr Cys Asp Asp Leu Phe Arg Phe Asn  
1 5 10 15

Asn Ile Asn Leu Asp Pro Leu Thr Thr Tyr Gly Ile Pro Phe Tyr  
20 25 30

Leu Gln Tyr Leu Ala His Trp Pro Glu Tyr Phe Ile Val Ala Glu Ala  
35 40 45

Pro Gly Gly Glu Leu Met Gly Tyr Ile Met Gly Lys Ala Glu Gly Ser  
50 55 60

Val Ala Arg Glu Glu Trp His Gly His Val Thr Ala Leu Ser Val Ala  
65 70 75 80

Pro Glu Phe Arg Arg Leu Gly Leu Ala Ala Lys Leu Met Glu Leu Leu  
85 90 95

Gln Glu Ile Ser Glu Arg Lys Gly Gly Phe Phe Val Asp Leu Phe Val  
100 105 110

Arg Val Ser Asn Gln Val Ala Val Asn Met Tyr Lys Gln Leu Gly Tyr  
115 120 125

Ser Val Tyr Arg Thr Val Ile Glu Tyr Tyr Ser Ala Ser Asn Gly Glu  
130 135 140

Pro Asp Glu Asp Ala Tyr Asp Met Arg Lys Ala Leu Ser Arg Asp Thr  
145 150 155 160

Glu Lys Lys Ser Ile Ile Pro Leu Pro His Pro Val Arg Pro Glu Asp  
165 170 175

Ile Glu

<210> 134

<211> 185

<212> PRT

<213> Homo sapiens

<400> 134

Met Gly Pro Glu Arg His Leu Ser Gly Ala Pro Ala Arg Met Ala Thr  
1 5 10 15

Val Val Leu Gly Gly Asp Thr Met Gly Pro Glu Arg Ile Phe Pro Asn  
20 25 30

Gln Thr Glu Glu Leu Gly His Gln Gly Pro Ser Glu Gly Thr Gly Asp  
35 40 45

Trp Ser Ser Glu Glu Pro Glu Glu Glu Glu Thr Gly Ser Gly  
50 55 60

Pro Ala Gly Tyr Ser Tyr Glu Pro Leu An Glu Asp Pro Glu Glu Glu  
65 70 75 80

Glu Val Glu Leu Ala Pro Val Gly Asp Gly Asp Val Val Ala Asp Ile  
85 90 95

Gln Asp Arg Ile Gln Ala Leu Glu Glu Glu Glu Thr Ala Leu An An His  
100 105 110 115

Glu Ser Glu Asp Glu Asp Glu Glu Glu Glu Thr Ala Leu An An His  
115 120 125

Ser Ser Ile Pro Met Asp Pro Glu His Val Glu Leu Val Lys Arg Thr  
130 135 140

Met Ala Gly Val Ser Leu Pro Ala Pro Gly Val Pro Ala Trp Ala Arg  
145 150 155 160

Glu Ile Ser Asp Ala Gln Trp Glu Asp Val Val Gln Lys Ala Leu Gln  
165 170 175

Ala Arg Gln Ala Ser Pro Ala Trp Lys  
180 185

<210> 135  
<211> 397  
<212> PRT  
<213> Homo sapiens  
<400> 135

Met An Ala Gly Ser Asp Pro Val Ile Val Ser Ala Ala Arg Thr  
1 5 10 15

Ile Ile Gly Ser Phe An Gly Ala Leu Ala Ala Val Pro Val Gln Asp  
20 25 30

Leu Gly Ser Thr Val Ile Lys Glu Val Leu Lys Arg Ala Thr Val Ala  
35 40 45

Pro Glu Asp Val Ser Glu Val Ile Phe Gly His Val Leu Ala Ala Gly  
50 55 60

Cys Gly Gln An Pro Val Arg Gln Ala Ser Val Gly Ala Gly Ile Pro  
65 70 75 80

Tyr Ser Val Pro Ala Trp Ser Cys Gln Met Ile Cys Gly Ser Gly Leu  
85 90 95

Lys Ala Val Cys Leu Ala Val Gln Ser Ile Gly Ile Gly Asp Ser Ser  
100 105 110

Ile Val Val Ala Gly Gly Met Glu An Met Ser Lys Ala Pro His Leu  
115 120 125

Ala Tyr Leu Arg Thr Gly Val Lys Ile Gly Glu Met Pro Leu Thr Asp  
130 135 140

Ser Ile Leu Cys Asp Gly Leu Thr Asp Ala Phe His An Cys His Met  
145 150 155 160

Gly Ile Thr Ala Glu An Val Ala Thr Lys Trp Gln Val Ser Arg Glu  
165 170 175

Asp Gln Asp Lys Val Ala Val Leu Ser Gln An Arg Thr Glu An Ala  
180 185 190

Gln Lys Ala Gly His Phe Asp Lys Glu Ile Val Pro Val Leu Val Ser  
195 200 205

Thr Arg Lys Gly Leu Ile Glu Val Lys Thr Asp Glu Phe Pro Arg His  
210 215 220

Gly Ser An Ile Glu Ala Met Ser Lys Leu Lys Pro Tyr Phe Leu Thr  
225 230 235 240

Asp Gly Thr Gly Thr Val Thr Pro Ala An Ala Ser Gly Ile An Asp  
245 250 255

Gly Ala Ala Ala Val Ala Leu Met Lys Lys Ser Glu Ala Asp Lys Arg  
260 265 270

Gly Leu Thr Pro Leu Ala Arg Ile Val Ser Trp Ser Gln Val Gly Val  
275 280 285

Glu Pro Ser Ile Met Gly Ile Gly Pro Ile Pro Ala Ile Lys Gln Ala  
290 295 300

Val Thr Lys Ala Gly Trp Ser Leu Glu Asp Val Asp Ile Phe Glu Ile  
305 310 315 320

An Glu Ala Phe Ala Ala Val Ser Ala Ala Ile Val Lys Glu Leu Gly  
325 330 335

Leu An Pro Glu Lys Val An Ile Glu Gly Gly Ala Ile Ala Leu Gly  
340 345 350

His Pro Leu Gly Ala Ser Gly Cys Arg Ile Leu Val Thr Leu Leu His  
355 360 365

Thr Leu Glu Arg Met Gly Arg Ser Arg Gly Val Ala Ala Leu Cys Ile  
370 375 380

Gly Gly Gly Met Gly Ile Ala Met Cys Val Gln Arg Glu  
385 390 395

<210> 136  
<211> 356  
<212> PRT  
<213> Homo sapiens  
<400> 136

Met Glu Gly Pro Leu Ser Val Phe Gly Asp Arg Ser Thr Gly Glu Thr  
1 5 10 15

Ile Arg Ser Gln An Val Met Ala Ala Ser Ile Ala An Ile Val  
20 25 30



Lys Ser Ser Leu Gly Pro Val Gly Leu Asp Lys Met Leu Val Asp Asp 45  
 35  
 Ile Gly Asp Val Thr Thr Asn Asp Gly Ala Thr Ile Leu Lys Leu 60  
 50  
 Leu Glu Val Glu His Pro Ala Ala Lys Val Leu Cys Glu Leu Ala Asp 80  
 65  
 Leu Glu Asp Lys Glu Val Gly Asp Gly Thr Thr Ser Val Val Ile Ile 95  
 85  
 Ala Ala Glu Leu Leu Lys Asn Ala Asp Glu Leu Val Lys Glu Lys Ile 110  
 100  
 His Pro Thr Ser Val Ile Ser Gly Tyr Arg Leu Ala Cys Lys Glu Ala 125  
 115  
 Val Arg Tyr Ile Asn Glu Asn Leu Ile Val Asn Thr Asp Glu Leu Gly 140  
 130  
 Arg Asp Cys Leu Ile Asn Ala Ala Lys Thr Ser Met Ser Ser Lys Ile 160  
 145  
 Ile Gly Ile Asn Gly Asp Phe Ala Asn Met Val Val Asp Ala Val 175  
 165  
 Leu Ala Ile Lys Tyr Thr Asp Ile Arg Gly Glu Pro Arg Tyr Pro Val 190  
 180  
 Asn Ser Val Asn Ile Leu Lys Ala His Gly Arg Ser Glu Met Glu Ser 205  
 195  
 Met Leu Ile Ser Gly Tyr Ala Leu Asn Cys Val Val Gly Ser Glu Gly 220  
 210  
 Met Pro Lys Arg Ile Val Asn Ala Lys Ile Ala Cys Leu Asp Phe Ser 240  
 225  
 Leu Glu Lys Thr Lys Met Lys Leu Gly Val Glu Val Val Ile Thr Asp 255  
 245  
 Pro Glu Lys Leu Asp Glu Ile Arg Glu Arg Glu Ser Asp Ile Thr Lys 270  
 260  
 Glu Arg Ile Glu Lys Ile Leu Ala Thr Gly Ala Asn Val Ile Leu Thr 285  
 275  
 Thr Gly Gly Ile Asp Asp Met Cys Leu Lys Tyr Phe Val Glu Ala Gly 300  
 290  
 Ala Met Ala Val Arg Arg Val Leu Lys Arg Asp Leu Lys Arg Ile Ala 320  
 305  
 Lys Ala Ser Gly Ala Thr Ile Leu Ser Thr Leu Ala Asn Leu Glu Gly 335  
 325  
 Glu Glu Thr Phe Glu Ala Ala Met Leu Gly Glu Ala Glu Val Val 350  
 340

Glu Glu Arg Ile Cys Asp Asp Glu Leu Ile Leu Ile Lys Asn Thr Lys 385  
 355  
 Ala Arg Thr Ser Ala Ser Ile Ile Leu Arg Gly Ala Asn Asp Phe Met 380  
 370  
 Cys Asp Glu Met Glu Arg Ser Leu His Asp Ala Leu Cys Val Val Lys 400  
 385  
 Arg Val Leu Glu Ser Lys Ser Val Val Pro Gly Gly Ala Val Glu 415  
 405  
 Ala Ala Leu Ser Ile Tyr Leu Glu Asn Tyr Ala Thr Ser Met Gly Ser 430  
 420  
 Arg Glu Glu Leu Ala Ile Ala Glu Phe Ala Arg Ser Leu Leu Val Ile 445  
 435  
 Pro Asn Thr Leu Ala Val Asn Ala Ala Glu Asp Ser Thr Asp Leu Val 460  
 450  
 Ala Lys Leu Arg Ala Phe His Asn Glu Ala Glu Val Asn Pro Glu Arg 480  
 465  
 Lys Asn Leu Lys Trp Ile Gly Leu Asp Leu Ser Asn Gly Lys Pro Arg 495  
 485  
 Asp Asn Lys Glu Ala Gly Val Phe Glu Pro Thr Ile Val Lys Val Lys 510  
 500  
 Ser Leu Lys Phe Ala Thr Glu Ala Ala Ile Thr Ile Leu Arg Ile Asp 525  
 515  
 Asn Leu Ile Lys Leu His Pro Glu Ile Leu Arg Ile Lys His Gly Ser 540  
 530  
 Tyr Glu Asp Ala Val His Ser Gly Ala Leu Asn Asp 555  
 545  
 <210> 137  
 <211> 266  
 <212> PRT  
 <213> Homo sapiens  
 <400> 137  
 Met Pro Lys Gly Lys Lys Ala Lys Gly Lys Lys Val Ala Pro Ala Pro 15  
 1  
 Ala Val Val Lys Lys Glu Glu Ala Lys Lys Val Val Asn Pro Leu Phe 30  
 20  
 Glu Lys Arg Pro Lys Asn Phe Gly Ile Gly Glu Asp Ile Glu Pro Lys 45  
 35  
 Arg Asp Leu Thr Arg Phe Val Lys Trp Pro Arg Tyr Ile Arg Leu Glu 60  
 50  
 Arg Glu Arg Ala Ile Leu Tyr Lys Arg Leu Lys Val Pro Pro Ala Ile 80  
 65

Asn Gln Phe Thr Thr Gln Ala Leu Asp Arg Gln Thr Ala Thr Gln Leu Leu 95  
85  
Lys Leu Ala His Lys Tyr Arg Pro Glu Thr Lys Gln Glu Lys Lys Gln 110  
100  
Arg Leu Leu Ala Arg Ala Glu Lys Lys Ala Ala Gly Lys Gly Asp Val 125  
115  
Pro Thr Lys Arg Pro Pro Val Leu Arg Ala Gly Val Asn Thr Val Thr 140  
130  
Thr Leu Val Glu Asn Lys Lys Ala Gln Leu Val Val Ile Ala His Asp 160  
145  
Val Asp Pro Ile Glu Leu Val Val Phe Leu Pro Ala Leu Cys Arg Lys 175  
165  
Met Gly Val Pro Tyr Cys Ile Ile Lys Gly Lys Ala Arg Leu Gly Arg 190  
180  
Leu Val His Arg Lys Thr Cys Thr Thr Val Ala Phe Thr Gln Val Asn 205  
195  
Ser Glu Asp Lys Gly Ala Leu Ala Lys Leu Val Glu Ala Ile Arg Thr 220  
210  
Asn Tyr Asn Asp Arg Tyr Asp Glu Ile Arg Arg His Trp Gly Gly Asn 235  
225  
Val Leu Gly Pro Lys Ser Val Ala Arg Ile Ala Lys Leu Glu Lys Ala 255  
245  
Lys Ala Lys Glu Leu Ala Thr Lys Leu Gly 265  
260  
<210> 138  
<211> 160  
<212> PRT  
<213> Homo sapiens  
<400> 138  
Met Asp Cys Gln Asn Gly His Gln His Ile Ser Gln Glu Leu Glu Val 1  
3  
Leu Arg Ile His Met Gln Leu Val Thr Val Gln Phe Thr Gln Leu Gly 20  
25  
Lys Gly Ala Leu Glu Ile Ile Gln Val Leu Cys Gly Ile Ser Gln Gly 35  
40  
Ser Gln His Leu Leu Ala Met Cys Leu Asp Phe Gly Val Ala His Asp 50  
55  
Gly Arg Gly Arg Gly Gln Val Ala Lys Ala Val Lys Glu Pro Leu Gly 65  
70  
Pro Trp Val Asp Asn Gln Glu Pro Ser Gln Gly Phe Ser Ser Ile 85  
90

Phe His Ile His Leu Ala Pro Gln Ala Cys Asp Ser Ser Leu Val Leu 100  
105  
Leu Cys Glu Met Thr His Gly Val Trp Thr Arg Ser Leu Leu Ile Thr 115  
120  
Ser Asp Val Pro Glu Ala Ser Val Thr Gln Ile Leu Leu Cys Ala Met 130  
135  
Trp Thr Leu Pro Ser His Ala Thr Thr Arg Glu Leu Thr Gln Trp Val 145  
150  
<210> 139  
<211> 172  
<212> PRT  
<213> Homo sapiens  
<400> 139  
Met Ile Ile Tyr Arg Asp Leu Ile Ser His Asp Glu Met Phe Ser Asp 1  
5  
Ile Tyr Lys Ile Arg Glu Ile Ala Asp Gly Leu Cys Leu Glu Val Glu 20  
25  
Gly Lys Met Val Ser Arg Thr Glu Gly Asn Ile Asp Asp Ser Leu Ile 35  
40  
Gly Gly Asn Ala Ser Ala Glu Gly Pro Glu Gly Glu Gly Thr Glu Ser 50  
55  
Thr Val Ile Thr Gly Val Asp Ile Val Met Asn His His Leu Gln Glu 65  
70  
Thr Ser Phe Thr Lys Glu Ala Tyr Lys Lys Tyr Ile Lys Asp Tyr Met 85  
90  
Lys Ser Ile Lys Gly Lys Leu Glu Gln Arg Pro Glu Arg Val Lys 100  
105  
Pro Phe Met Thr Gly Ala Ala Glu Gln Ile Lys His Ile Leu Ala Asn 115  
120  
Phe Lys Asn Tyr Gln Phe Phe Ile Gly Glu Asn Met Asn Pro Asp Gly 130  
135  
Met Val Ala Leu Leu Asp Tyr Arg Glu Asp Gly Val Thr Pro Tyr Met 145  
150  
Ile Phe Phe Lys Asp Gly Leu Glu Met Glu Lys Cys 165  
170  
<210> 140  
<211> 133  
<212> PRT  
<213> Homo sapiens  
<400> 140  
Met Asn Asp Thr Val Thr Ile Arg Thr Arg Lys Phe Met Thr Asn Arg 1  
5  
10

Leu Leu Gln Arg Lys Gln Met Val Ile Asp Val Leu Leu His Pro Lys Lys 25 30  
Ala Thr Val Pro Lys Thr Glu Ile Arg Glu Lys Leu Ala Lys Met Tyr 35 45  
Lys Thr Thr Pro Asp Val Ile Phe Val Phe Gly Phe Arg Thr His Phe 50 60  
Gly Gly Gly Lys Thr Thr Gly Phe Gly Met Ile Tyr Asp Ser Leu Asp 65 75  
Tyr Ala Lys Lys Asn Glu Pro Lys His Arg Leu Ala Arg His Gly Leu 80 95  
Tyr Glu Lys Lys Lys Thr Ser Arg Lys Gln Arg Lys Glu Arg Lys Asn 100 110  
Arg Met Lys Lys Val Arg Gly Thr Ala Lys Ala Asn Val Gly Ala Gly 115 125  
Lys Lys Pro Lys Glu 130  
<210> 141  
<211> 404  
<212> PRT  
<213> Homo sapiens  
<400> 141  
Met Asn Ile Val Glu Asn Ser Ile Phe Leu Ser Asn Leu Met Lys Ser 1 15  
Ala Tyr Thr Tyr Ser Thr Phe Pro Ala Gly Val Pro Val Ser Glu Arg 20 30  
Met Ser Thr Tyr Ser Thr Phe Pro Ala Gly Val Pro Val Ser Glu Arg 35 45  
Ser Leu Ala Arg Ala Gly Phe Tyr Tyr Thr Gly Val Asn Asp Lys Val 50 60  
Lys Cys Phe Cys Cys Gly Leu Met Leu Asp Asn Trp Lys Arg Gly Asp 65 75  
Ser Pro Thr Glu Lys His Lys Lys Leu Tyr Pro Ser Cys Arg Phe Val 80 95  
Gln Ser Leu Asn Ser Val Asn Asn Leu Glu Ala Thr Ser Gln Pro Thr 100 110  
Phe Pro Ser Ser Val Thr Asn Ser Thr His Ser Leu Leu Pro Gly Thr 115 125  
Glu Asn Ser Gly Tyr Phe Arg Gly Ser Tyr Ser Asn Ser Pro Ser Asn 130 140  
Pro Val Asn Ser Arg Ala Asn Gln Asp Phe Ser Ala Leu Met Arg Ser 145 155

Ser Tyr His Cys Ala Met Asn Asn Glu Asn Ala Arg Leu Leu Tyr Phe 165 175  
Gln Thr Trp Pro Leu Thr Phe Leu Ser Pro Thr Asp Leu Ala Lys Ala 180 190  
Gly Phe Tyr Tyr Ile Gly Pro Gly Asp Arg Val Ala Cys Phe Ala Cys 195 205  
Gly Gly Lys Leu Ser Asn Trp Glu Pro Lys Asp Asn Ala Met Ser Glu 210 220  
His Leu Arg His Phe Pro Lys Cys Pro Phe Ile Glu Asn Gln Leu Gln 225 235  
Asp Thr Ser Arg Tyr Thr Val Ser Asn Leu Ser Met Gln Thr His Ala 240 255  
Ala Arg Phe Lys Thr Phe Phe Asn Trp Pro Ser Ser Val Leu Val Asn 260 270  
Pro Glu Gln Leu Ala Ser Ala Gly Phe Tyr Tyr Val Gly Asn Ser Asp 275 285  
Asp Val Lys Cys Phe Cys Asp Gly Gly Leu Arg Cys Trp Glu Ser 290 300  
Gly Asp Asp Pro Trp Val Gln His Ala Lys Trp Phe Pro Arg Cys Glu 305 315  
Tyr Leu Ile Arg Ile Lys Gly Gln Glu Phe Ile Arg Gln Val Gln Ala 320 335  
Ser Tyr Pro His Leu Leu Glu Gln Leu Ser Thr Ser Asp Ser Pro 340 350  
Gly Asp Glu Asn Ala Glu Ser Ser Ile Ile His Phe Glu Pro Gly Glu 355 365  
Asp His Ser Glu Asp Ala Ile Met Met Asn Thr Pro Val Ile Asn Ala 370 380  
Ala Val Glu Met Gly Phe Ser Arg Ser Leu Val Lys Gln Thr Val Gln 385 395  
Arg Lys Ile Leu Ala Thr Gly Glu Asn Tyr Arg Leu Val Asn Asp Leu 400 415  
Val Leu Asp Leu Leu Asn Ala Glu Asp Glu Ile Arg Glu Glu Arg 420 430  
Glu Arg Ala Thr Glu Glu Lys Glu Ser Asn Asp Leu Leu Ile Arg 435 445  
Lys Asn Arg Met Ala Leu Phe Gln His Leu Thr Cys Val Ile Pro Ile 450 460  
Leu Asp Ser Leu Leu Thr Ala Gly Ile Ile Asn Glu Gln Glu His Asp 465 475

Val Ile Lys Glu Lys Thr Gln Thr Ser Leu Gln Ala Arg Glu Leu Ile 495  
485  
Asp Thr Ile Leu Val Lys Gly Asn Ile Ala Ala Thr Val Phe Arg Asn 510  
500  
Ser Leu Gln Glu Ala Glu Ala Val Leu Tyr Glu His Leu Phe Val Gln 525  
515  
Gln Asp Ile Lys Tyr Ile Pro Thr Glu Asp Val Ser Asp Leu Pro Val 540  
530  
Glu Glu Gln Leu Arg Arg Leu Gln Glu Glu Arg Thr Cys Lys Val Cys 560  
545  
Met Asp Lys Glu Val Ser Ile Val Phe Ile Pro Cys Gly His Leu Val 575  
565  
Val Cys Lys Asp Cys Ala Pro Ser Leu Arg Lys Cys Pro Ile Cys Arg 590  
580  
Ser Thr Ile Lys Gly Thr Val Arg Thr Phe Leu Ser 600  
595  
<210> 142  
<211> 624  
<212> PRT  
<213> Homo sapiens  
<400> 142  
Met Gln Pro Asp Pro Arg Pro Ser Gly Ala Gly Ala Cys Cys Arg Phe 15  
1  
5  
10  
Leu Pro Leu Gln Ser Gln Cys Pro Glu Gly Ala Gly Asp Ala Val Met 30  
20  
25  
Tyr Ala Ser Thr Glu Cys Lys Ala Glu Val Thr Pro Ser Gln His Gly 45  
35  
40  
Asn Arg Thr Phe Ser Tyr Thr Leu Glu Asp His Thr Lys Gln Ala Phe 60  
50  
55  
Gly Ile Met Asn Glu Leu Arg Leu Ser Gln Leu Cys Asp Val Thr 80  
65  
70  
75  
Leu Gln Val Lys Tyr Gln Asp Ala Pro Ala Ala Gln Phe Met Ala His 95  
80  
85  
Lys Val Val Leu Ala Ser Ser Ser Pro Val Phe Lys Ala Met Phe Thr 110  
100  
105  
Asn Gly Leu Arg Glu Gln Gly Met Glu Val Val Ser Ile Glu Gly Ile 125  
115  
120  
His Pro Lys Val Met Glu Arg Leu Ile Glu Phe Ala Tyr Thr Ala Ser 140  
130  
135  
Ile Ser Met Gly Glu Lys Cys Val Leu His Val Met Asn Gly Ala Val 160  
145  
150  
155

Met Tyr Gln Ile Asp Ser Val Val Arg Ala Cys Ser Asp Phe Leu Val 175  
165  
170  
Gln Gln Leu Asp Pro Ser Asn Ala Ile Gly Ile Ala Asn Phe Ala Glu 190  
180  
185  
Gln Ile Gly Cys Val Glu Leu His Gln Arg Ala Arg Glu Tyr Ile Tyr 205  
195  
200  
Met His Phe Gly Glu Val Ala Lys Gln Glu Glu Phe Phe Asn Leu Ser 220  
210  
215  
His Cys Gln Leu Val Thr Leu Ile Ser Arg Asp Asn Leu Val Arg 240  
225  
230  
Cys Glu Ser Glu Val Phe His Ala Cys Ile Asn Trp Val Lys Tyr Asp 255  
245  
250  
Cys Glu Gln Arg Arg Phe Tyr Val Gln Ala Leu Leu Arg Ala Val Arg 270  
260  
265  
Cys His Ser Leu Thr Pro Asn Phe Leu Gln Met Gln Leu Gln Lys Cys 285  
275  
280  
Glu Ile Leu Gln Ser Asp Ser Arg Cys Lys Asp Tyr Leu Val Lys Ile 300  
290  
295  
Phe Glu Glu Leu Thr Leu His Lys Pro Thr Gln Val Met Pro Cys Arg 320  
305  
310  
Ala Pro Lys Val Gly Arg Leu Ile Tyr Thr Ala Gly Gly Tyr Phe Arg 335  
325  
330  
Gln Ser Leu Ser Tyr Leu Glu Ala Tyr Asn Pro Ser Asn Gly Thr Trp 350  
340  
345  
Leu Arg Leu Ala Asp Leu Gln Val Pro Arg Ser Gly Leu Ala Gly Cys 365  
355  
360  
Val Val Gly Gly Leu Leu Tyr Ala Val Gly Gly Arg Asn Asn Ser Pro 380  
370  
375  
Asp Gly Asn Thr Asp Ser Ser Ala Leu Asp Cys Tyr Asn Pro Met Thr 400  
385  
390  
Asn Gln Trp Ser Pro Cys Ala Pro Met Ser Val Pro Arg Asn Arg Ile 415  
405  
410  
Gly Val Gly Val Ile Asp Gly His Ile Tyr Ala Val Gly Gly Ser His 430  
420  
425  
Gly Cys Ile His Asn Ser Val Glu Arg Tyr Glu Pro Glu Arg Asp 445  
435  
440  
Glu Trp His Leu Val Ala Pro Met Leu Thr Arg Arg Ile Gly Val Gly 460  
450  
455  
Val Ala Val Leu Asn Arg Leu Leu Tyr Ala Val Gly Gly Phe Asp Gly 480  
465  
470  
475

Thr Asn Arg Leu Asn Ser Ala Glu Cys Tyr Tyr Pro Glu Arg Asn Glu  
485 490 495

Trp Arg Met Ile Thr Ala Met Asn Thr Ile Arg Ser Gly Ala Gly Val  
500 505 510

Cys Val Leu His Asn Cys Ile Tyr Ala Ala Gly Gly Tyr Asp Gly Gln  
515 520 525

Asp Gln Leu Asn Ser Val Glu Arg Tyr Asp Val Glu Thr Glu Thr Trp  
530 535 540

Thr Phe Val Ala Pro Met Lys His Arg Arg Ser Ala Leu Gly Ile Thr  
545 550 555

Val His Gln Gly Arg Ile Tyr Val Leu Gly Gly Tyr Asp Gly His Thr  
565 570 575

Phe Leu Asp Ser Val Glu Cys Tyr Asp Pro Asp Thr Asp Thr Trp Ser  
580 585 590

Glu Val Thr Arg Met Thr Ser Gly Arg Ser Gly Val Gly Val Ala Val  
595 600 605

Thr Met Glu Pro Cys Arg Lys Gln Ile Asp Gln Gln Asn Cys Thr Cys  
610 615 620

<210> 143  
<211> 389  
<212> PRT  
<213> Homo sapiens

Met Leu Ser Leu Arg Val Pro Leu Ala Pro Ile Thr Asp Pro Gln Gln  
1 5 10 15

Leu Gln Leu Ser Pro Leu Lys Gly Leu Ser Leu Val Asp Lys Glu Asn  
20 25 30

Thr Pro Pro Ala Leu Ser Gly Thr Arg Val Leu Ala Ser Lys Thr Ala  
35 40 45

Arg Arg Ile Phe Gln Glu Pro Thr Glu Pro Lys Thr Lys Ala Ala  
50 55 60

Pro Gly Val Glu Asp Glu Pro Leu Leu Arg Glu Asn Pro Arg Arg Phe  
65 70 75

Val Ile Phe Pro Ile Glu Tyr His Asp Ile Trp Gln Met Tyr Lys Lys  
85 90 95

Ala Glu Ala Ser Phe Trp Thr Ala Glu Glu Val Asp Leu Ser Lys Asp  
100 105 110

Ile Gln His Trp Glu Ser Leu Lys Pro Glu Glu Arg Tyr Phe Ile Ser  
115 120 125

His Val Leu Ala Phe Phe Ala Ala Ser Asp Gly Ile Val Asn Glu Asn  
130 135 140

Leu Val Glu Arg Phe Ser Gln Glu Val Gln Ile Thr Glu Ala Arg Cys  
145 150 155

Phe Tyr Gly Phe Gln Ile Ala Met Glu Asn Ile His Ser Glu Met Tyr  
165 170 175

Ser Leu Leu Ile Asp Thr Tyr Ile Lys Asp Pro Lys Glu Arg Glu Phe  
180 185 190

Leu Phe Asn Ala Ile Glu Thr Met Pro Cys Val Lys Lys Lys Ala Asp  
195 200 205

Trp Ala Leu Arg Arg Trp Ile Gly Asp Lys Glu Ala Thr Tyr Gly Glu Arg  
210 215 220

Val Val Ala Phe Ala Val Glu Gly Ile Phe Phe Ser Ser Gly Ser Phe  
225 230 235

Ala Ser Ile Phe Trp Leu Lys Lys Arg Gly Leu Met Pro Gly Leu Thr  
245 250 255

Phe Ser Asn Glu Leu Ile Ser Arg Asp Glu Gly Leu His Cys Asp Phe  
260 265 270

Ala Cys Leu Met Phe Lys His Leu Val His Lys Pro Ser Glu Glu Arg  
275 280 285

Val Arg Glu Ile Ile Ile Asn Ala Val Arg Ile Glu Gln Glu Phe Leu  
290 295 300

Thr Glu Ala Leu Pro Val Lys Leu Ile Gly Met Asn Cys Thr Leu Met  
305 310 315

Lys Gln Tyr Ile Glu Phe Val Ala Asp Arg Leu Met Leu Glu Leu Gly  
325 330 335

Phe Ser Lys Val Phe Arg Val Glu Asn Pro Phe Asp Phe Met Glu Asn  
340 345 350

Ile Ser Leu Glu Gly Lys Thr Asn Phe Phe Glu Lys Arg Val Gly Glu  
355 360 365

Tyr Gln Arg Met Gly Val Met Ser Ser Pro Thr Glu Asn Ser Phe Thr  
370 375 380

Leu Asp Ala Asp Phe  
385

<210> 144  
<211> 281  
<212> PRT  
<213> Homo sapiens

<400> 144  
Met Ala Thr Asn Phe Leu Ala His Glu Lys Ile Trp Phe Asp Lys Phe  
1 5 10 15

Lys Tyr Asp Asp Ala Glu Arg Arg Phe Tyr Glu Gln Met Asn Gly Pro  
20 25 30

Val Arg Gly Ala Ser Arg Gln Glu Asn Gly Ala Thr Val Ile Leu Arg  
35 40 45  
Asp Ile Ala Arg Ala Arg Glu Asn Ile Gln Lys Ser Leu Ala Gly Ser  
50 55 60  
Ser Gly Pro Gly Ala Ser Ser Gly Thr Ser Gly Asp His Gly Glu Leu  
65 70 75 80  
Val Val Arg Ile Ala Ser Leu Glu Val Glu Asn Gln Ser Leu Arg Gly  
85 90 95  
Val Val Gln Glu Leu Gln Gln Ala Ile Ser Lys Leu Glu Ala Arg Leu  
100 105 110  
Asn Val Leu Glu Lys Ser Ser Pro Gly His Arg Ala Thr Ala Pro Gln  
115 120 125  
Thr Gln His Val Ser Pro Met Arg Gln Val Glu Pro Pro Ala Lys Lys  
130 135 140  
Pro Ala Thr Pro Ala Glu Asp Asp Glu Asp Asp Ile Asp Leu Phe  
145 150 155 160  
Gly Ser Asp Asn Glu Glu Glu Asp Lys Glu Ala Ala Gln Leu Arg Glu  
165 170 175  
Glu Arg Leu Arg Gln Tyr Ala Glu Lys Lys Ala Lys Lys Pro Ala Leu  
180 185 190  
Val Ala Lys Ser Ser Ile Leu Leu Asp Val Lys Pro Trp Asp Asp Glu  
195 200 205  
Thr Asp Met Ala Gln Leu Glu Ala Cys Val Arg Ser Ile Gln Leu Asp  
210 215 220  
Gly Leu Val Trp Gly Ala Ser Lys Leu Val Pro Val Gly Tyr Gly Ile  
225 230 235 240  
Arg Lys Leu Gln Ile Gln Cys Val Val Glu Asp Asp Lys Val Gly Thr  
245 250 255  
Asp Leu Leu Glu Glu Glu Ile Thr Lys Phe Glu Glu His Val Gln Ser  
260 265 270  
Val Asp Ile Ala Ala Phe Asn Lys Ile  
275 280  
<210> 145  
<211> 269  
<212> PRT  
<213> Homo sapiens  
<400> 145  
Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp  
1 5 10 15  
Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His  
20 25 30

Leu Val Leu Arg Leu Arg Gly Gly Met Gln Ile Phe Val Lys Thr Leu  
35 40 45  
Thr Gly Lys Thr Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile Glu  
50 55 60  
Asn Val Lys Ala Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln  
65 70 75 80  
Gln Arg Leu Ile Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu  
85 90 95  
Ser Asp Tyr Asn Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu Arg  
100 105 110  
Leu Arg Gly Gly Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr  
115 120 125  
Ile Thr Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala  
130 135 140  
Lys Ile Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile  
145 150 155 160  
Phe Ala Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn  
165 170 175  
Ile Gln Lys Glu Ser Thr Leu His Leu Val Leu Arg Glu Gly Gly  
180 185 190  
Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu  
195 200 205  
Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp  
210 215 220  
Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys  
225 230 235 240  
Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu  
245 250 255  
Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Val  
260 265 270  
<210> 146  
<211> 2231  
<212> PRT  
<213> Homo sapiens  
<400> 146  
Met Arg Leu Leu Ala Lys Ile Ile Cys Leu Met Leu Trp Ala Ile Cys  
1 5 10 15  
Val Ala Glu Asp Cys Asn Glu Leu Pro Pro Arg Arg Asn Thr Glu Ile  
20 25 30  
Leu Thr Gly Ser Trp Ser Asp Gln Thr Tyr Pro Glu Gly Thr Gln Ala  
35 40 45

Ile Tyr Lys Cys Arg Pro Gly Tyr Arg Ser Leu Gly Asn Val Ile Met  
50 55 60

Val Cys Arg Lys Gly Glu Trp Val Ala Leu Asn Pro Leu Arg Lys Cys  
65 70 75 80

Gln Lys Arg Pro Cys Gly His Pro Gly Asp Thr Phe Gly Thr Phe  
85 90 95

Thr Leu Thr Gly Gly Asn Val Phe Glu Tyr Gly Val Lys Ala Val Tyr  
100 105 110

Thr Cys Asn Glu Gly Tyr Gln Leu Leu Gly Glu Ile Asn Tyr Arg Glu  
115 120 125

Cys Asp Thr Asp Gly Trp Thr Asn Asp Ile Pro Ile Cys Glu Val Val  
130 135 140

Lys Cys Leu Pro Val Thr Ala Pro Glu Asn Gly Lys Ile Val Ser Ser  
145 150 155 160

Ala Met Glu Pro Asp Arg Glu Tyr His Phe Gly Gln Ala Val Arg Phe  
165 170 175

Val Cys Asn Ser Gly Tyr Lys Ile Glu Gly Asp Glu Glu Met His Cys  
180 185 190

Ser Asp Asp Gly Phe Trp Ser Lys Glu Lys Pro Lys Cys Val Glu Ile  
195 200 205

Ser Cys Lys Ser Pro Asp Val Ile Asn Gly Ser Pro Ile Ser Gln Lys  
210 215 220

Ile Ile Tyr Lys Glu Asn Glu Arg Phe Gln Tyr Lys Cys Asn Met Gly  
225 230 235 240

Tyr Glu Tyr Ser Glu Arg Gly Asp Ala Val Cys Thr Glu Ser Gly Trp  
245 250 255

Arg Pro Leu Pro Ser Cys Glu Glu Lys Ser Cys Asp Asn Pro Tyr Ile  
260 265 270

Pro Asn Gly Asp Tyr Ser Pro Leu Arg Ile Lys His Arg Thr Gly Asp  
275 280 285

Glu Ile Thr Tyr Gln Cys Arg Asn Gly Phe Tyr Pro Ala Thr Arg Gly  
290 295 300

Asn Thr Ala Lys Cys Thr Ser Thr Gly Trp Ile Pro Ala Pro Arg Cys  
305 310 315 320

Thr Leu Lys Pro Cys Asp Tyr Pro Asp Ile Lys His Gly Gly Leu Tyr  
325 330 335

His Glu Asn Met Arg Arg Pro Tyr Phe Pro Val Ala Val Gly Lys Tyr  
340 345 350

Tyr Ser Tyr Tyr Cys Asp Glu His Phe Glu Thr Pro Ser Gly Ser Tyr  
355 360 365

355 360 365

Trp Asp His Ile His Cys Thr Gln Asp Gly Trp Ser Pro Ala Val Pro  
370 375 380

Cys Leu Arg Lys Cys Tyr Phe Pro Tyr Leu Glu Asn Gly Tyr Asn Gln  
385 390 395 400

Asn His Gly Arg Lys Phe Val Gln Gly Lys Ser Ile Asp Val Ala Cys  
405 410 415

His Pro Gly Tyr Ala Leu Pro Lys Ala Gln Thr Thr Val Thr Cys Met  
420 425 430

Glu Asn Gly Trp Ser Pro Thr Pro Arg Cys Ile Arg Val Lys Thr Cys  
435 440 445

Ser Lys Ser Ser Ile Asp Ile Glu Asn Gly Phe Ile Ser Glu Ser Gln  
450 455 460

Tyr Thr Tyr Ala Leu Lys Glu Lys Ala Lys Tyr Gln Cys Lys Leu Gly  
465 470 475 480

Tyr Val Thr Ala Asp Gly Glu Thr Ser Gly Ser Ile Arg Cys Gly Lys  
485 490 495

Asp Gly Trp Ser Ala Gln Pro Thr Cys Ile Lys Ser Cys Asp Ile Pro  
500 505 510

Val Phe Met Asn Ala Arg Thr Lys Asn Asp Phe Thr Trp Phe Lys Leu  
515 520 525

Asn Asp Thr Leu Asp Tyr Glu Cys His Asp Gly Tyr Glu Ser Asn Thr  
530 535 540

Gly Ser Thr Thr Gly Ser Ile Val Cys Gly Tyr Asn Gly Trp Ser Asp  
545 550 555 560

Leu Pro Ile Cys Tyr Glu Arg Glu Cys Glu Leu Pro Lys Ile Asp Val  
565 570 575

His Leu Val Pro Asp Arg Lys Lys Asp Gln Tyr Lys Val Gly Glu Val  
580 585 590

Leu Lys Phe Ser Cys Lys Pro Gly Phe Thr Ile Val Gly Pro Asn Ser  
595 600 605

Val Gln Cys Tyr His Phe Gly Leu Ser Pro Asp Leu Pro Ile Cys Lys  
610 615 620

Glu Gln Val Gln Ser Cys Gly Pro Pro Glu Leu Leu Asn Gly Asn  
625 630 635 640

Val Lys Glu Lys Thr Lys Glu Glu Tyr Tyr His Ser Glu Val Val Glu  
645 650 655

Tyr Tyr Cys Asn Pro Arg Phe Leu Met Lys Gly Pro Asn Lys Ile Gln  
660 665 670

Cys Val Asp Gly Glu Trp Thr Thr Leu Glu Val Cys Lys Val Val Val Val  
675 680 685

Ser Thr Cys Gly Asp Ile Pro Glu Leu Glu His Gly Trp Ala Gln Leu  
690 695 700

Ser Ser Pro Pro Tyr Tyr Tyr Gly Asp Ser Val Glu Phe Asn Cys Ser  
705 710 715

Glu Ser Phe Thr Met Ile Gly His Arg Ser Ile Thr Cys Ile His Gly  
725 730 735

Val Trp Thr Glu Leu Pro Gln Cys Val Ala Ile Asp Lys Leu Lys Lys  
740 745 750

Cys Lys Ser Ser Asn Leu Ile Ile Leu Glu Glu His Leu Lys Asn Lys  
755 760 765

Lys Glu Phe Asp His Asn Ser Asn Ile Arg Tyr Arg Cys Arg Gly Lys  
770 775 780

Glu Gly Trp Ile His Thr Val Cys Ile Asn Gly Arg Trp Asp Pro Glu  
785 790 795 800

Val Asn Cys Ser Met Ala Gln Ile Gln Leu Cys Pro Pro Pro Gln  
805 810 815

Ile Pro Asn Ser His Asn Met Thr Thr Thr Leu Asn Tyr Arg Asp Gly  
820 825 830

Glu Lys Val Ser Val Leu Cys Gln Glu Asn Tyr Leu Ile Gln Glu Gly  
835 840 845

Glu Glu Ile Thr Cys Lys Asp Gly Arg Trp Gln Ser Ile Pro Leu Cys  
850 855 860

Val Glu Lys Ile Pro Cys Ser Gln Pro Pro Gln Ile Glu His Gly Thr  
865 870 875 880

Ile Asn Ser Ser Arg Ser Ser Gln Glu Ser Tyr Ala His Gly Thr Lys  
885 890 895

Leu Ser Tyr Thr Cys Glu Gly Gly Phe Arg Ile Ser Glu Glu Asn Glu  
900 905 910

Thr Thr Cys Tyr Met Gly Lys Trp Ser Ser Pro Pro Gln Cys Glu Gly  
915 920 925

Leu Pro Cys Lys Ser Pro Pro Glu Ile Ser His Gly Val Val Ala His  
930 935 940

Met Ser Asp Ser Tyr Gln Tyr Gly Glu Val Thr Tyr Lys Cys Phe  
945 950 955

Glu Gly Phe Gly Ile Asp Gly Pro Ala Ile Ala Lys Cys Leu Gly Glu  
965 970 975

Lys Trp Ser His Pro Pro Ser Cys Ile Lys Thr Asp Cys Leu Ser Leu  
980 985 990

Pro Ser Phe Glu Asn Ala Ile Pro Met Gly Glu Lys Lys Asp Val Tyr  
995 1000 1005

Lys Ala Gly Glu Gln Val Thr Tyr Thr Cys Ala Thr Tyr Tyr Lys  
1010 1015 1020

Met Asp Gly Ala Ser Asn Val Thr Cys Ile Asn Ser Arg Trp Thr  
1025 1030 1035

Gly Arg Pro Thr Cys Arg Asp Thr Ser Cys Val Asn Pro Pro Thr  
1040 1045 1050

Val Gln Asn Ala Tyr Ile Val Ser Arg Gln Met Ser Lys Tyr Pro  
1055 1060 1065

Ser Gly Glu Arg Val Arg Tyr Gln Cys Arg Ser Pro Tyr Glu Met  
1070 1075 1080

Phe Gly Asp Glu Glu Val Met Cys Leu Asn Gly Asn Trp Thr Glu  
1085 1090 1095

Pro Pro Gln Cys Lys Asp Ser Thr Gly Lys Cys Gly Pro Pro Pro  
1100 1105 1110

Pro Ile Asp Asn Gly Asp Ile Thr Ser Phe Pro Leu Ser Val Tyr  
1115 1120 1125

Ala Pro Ala Ser Ser Val Glu Tyr Gln Cys Gln Asn Leu Tyr Gln  
1130 1135 1140

Leu Glu Gly Asn Lys Arg Ile Thr Cys Arg Asn Gly Gln Trp Ser  
1145 1150 1155

Glu Pro Pro Lys Cys Leu His Pro Cys Val Ile Ser Arg Glu Ile  
1160 1165 1170

Met Glu Asn Tyr Asn Ile Ala Leu Arg Trp Thr Ala Lys Gln Lys  
1175 1180 1185

Leu Tyr Ser Arg Thr Gly Glu Ser Val Glu Phe Val Cys Lys Arg  
1190 1195 1200

Gly Tyr Arg Leu Ser Ser Arg Ser His Thr Leu Arg Thr Thr Cys  
1205 1210 1215

Trp Asp Gly Lys Leu Glu Tyr Pro Thr Cys Ala Lys Arg  
1220 1225 1230

<210> 147  
<211> 364  
<212> PRT  
<213> Homo sapiens  
<400> 147

Met Tyr Leu Ser Arg Phe Leu Ser Ile His Ala Leu Trp Val Thr Val  
1 5 10 15

Ser Ser Val Met Gln Pro Tyr Pro Leu Val Trp Gly His Tyr Asp Leu  
20 25 30



Cys Lys Thr Gln Ile Tyr Thr Glu Glu Gly Lys Val Trp Asp Tyr Met 35 40 45  
Ala Cys Gln Pro Glu Ser Thr Asp Met Thr Lys Tyr Leu Lys Val Lys 50 55 60  
Leu Asp Pro Pro Asp Ile Thr Cys Gly Asp Pro Pro Glu Thr Phe Cys 65 70 75 80  
Ala Met Gly Asn Pro Tyr Met Cys Asn Asn Glu Cys Asp Ala Ser Thr 85 90 95  
Pro Glu Leu Ala His Pro Pro Glu Leu Met Phe Asp Phe Glu Gly Arg 100 105 110  
His Pro Ser Thr Phe Trp Gln Ser Ala Thr Trp Lys Glu Tyr Pro Lys 115 120 125  
Pro Leu Gln Val Asn Ile Thr Leu Ser Trp Ser Lys Thr Ile Glu Leu 130 135 140  
Thr Asp Asn Ile Val Ile Thr Phe Glu Ser Gly Arg Pro Asp Gln Met 145 150 155 160  
Ile Leu Glu Lys Ser Leu Asp Tyr Gly Arg Thr Trp Gln Pro Tyr Gln 165 170 175  
Tyr Tyr Ala Thr Asp Cys Leu Asp Ala Phe His Met Asp Pro Lys Ser 180 185 190  
Val Lys Asp Leu Ser Gln His Thr Val Leu Glu Ile Ile Cys Thr Glu 195 200 205  
Glu Tyr Ser Thr Gly Tyr Thr Thr Asn Ser Lys Ile Ile His Phe Glu 210 215 220  
Ile Lys Asp Arg Phe Ala Phe Phe Ala Gly Pro Arg Leu Arg Asn Met 225 230 235 240  
Ala Ser Leu Tyr Gly Gln Leu Asp Thr Thr Lys Lys Leu Arg Asp Phe 245 250 255  
Phe Thr Val Thr Asp Leu Arg Ile Arg Leu Leu Arg Pro Ala Val Gly 260 265 270  
Glu Ile Phe Val Asp Glu Leu His Leu Ala Arg Tyr Phe Tyr Ala Ile 275 280 285  
Ser Asp Ile Lys Val Arg Gly Arg Cys Lys Cys Asn Leu His Ala Thr 290 295 300  
Val Cys Val Tyr Asp Asn Ser Lys Leu Thr Cys Glu Cys Glu His Asn 305 310 315 320  
Thr Gly Pro Asp Cys Gly Lys Cys Lys Lys Asn Tyr Gln Gly Arg 325 330 335  
Pro Trp Ser Pro Gly Ser Tyr Leu Pro Ile Pro Lys Gly Thr Ala Asn 340 345 350

Thr Cys Ile Pro Ser Ile Ser Ser Ile Gly Ser Lys 355 360

<210> 148  
<211> 3210  
<212> PRT  
<213> Homo sapiens

<400> 148

Met Ser Trp Ala Leu Glu Glu Trp Lys Glu Gly Leu Pro Thr Arg Thr 1 5 10 15

Leu Gln Lys Ile Gln Glu Leu Glu Gly Gln Leu Asp Lys Leu Lys Lys 20 25 30

Glu Lys Gln Gln Arg Gln Phe Gln Leu Asp Ser Leu Glu Ala Ala Pro 35 40 45

Gln Lys Gln Thr Gln Lys Val Glu Asn Glu Lys Thr Glu Gly Thr Asn 50 55 60

Leu Lys Arg Glu Asn Gln Arg Leu Met Glu Ile Cys Glu Ser Leu Glu 65 70 75 80

Lys Thr Lys Gln Lys Ile Ser His Glu Leu Gln Val Lys Glu Ser Gln 85 90 95

Val Asn Phe Gln Glu Gly Gln Leu Asn Ser Gly Lys Lys Gln Ile Glu 100 105 110

Lys Leu Glu Gln Glu Leu Lys Arg Cys Lys Ser Glu Leu Glu Arg Ser 115 120 125

Gln Gln Ala Ala Gln Ser Ala Asp Val Ser Leu Asn Pro Cys Asn Thr 130 135 140

Pro Gln Lys Ile Phe Thr Thr Pro Leu Thr Pro Ser Gln Tyr Tyr Ser 145 150 155 160

Gly Ser Lys Tyr Glu Asp Leu Lys Glu Lys Tyr Asn Lys Glu Val Glu 165 170 175

Glu Arg Lys Arg Leu Glu Ala Glu Val Lys Ala Leu Gln Ala Lys Lys 180 185 190

Ala Ser Gln Thr Leu Pro Gln Ala Thr Met Asn His Arg Asp Ile Ala 195 200 205

Arg His Gln Ala Ser Ser Ser Val Phe Ser Trp Gln Gln Glu Lys Thr 210 215 220

Pro Ser His Leu Ser Ser Asn Ser Gln Arg Thr Pro Ile Arg Arg Asp 225 230 235 240

Phe Ser Ala Ser Tyr Phe Ser Gly Glu Leu Glu Val Thr Pro Ser Arg 245 250 255

Ser Thr Leu Gln Ile Gly Lys Arg Asp Ala Asn Ser Ser Phe Phe Gly 260 265 270

Asn Ser Ser Ser Pro His Leu Leu Asp Gln Lys Ala Gln Asn Gln 275 280 285  
 Glu Leu Arg Asn Lys Ile Asn Glu Leu Glu Leu Arg Leu Gln Gly His 290 295 300  
 Glu Lys Glu Met Lys Gly Gln Val Asn Lys Phe Gln Glu Leu Gln Leu 305 310 315  
 Gln Leu Glu Lys Ala Lys Val Glu Leu Ile Glu Lys Glu Lys Val Leu 320 325 330 335  
 Asn Lys Cys Arg Asp Glu Leu Val Arg Thr Thr Ala Gln Tyr Asp Gln 340 345 350  
 Ala Ser Thr Lys Tyr Thr Ala Leu Glu Gln Lys Leu Lys Leu Thr 355 360 365  
 Glu Asp Leu Ser Cys Gln Arg Gln Asn Ala Glu Ser Ala Arg Cys Ser 370 375 380  
 Leu Glu Gln Lys Ile Lys Glu Lys Glu Lys Glu Phe Gln Glu Glu Leu 385 390 395 400  
 Ser Arg Gln Gln Arg Ser Phe Gln Thr Leu Asp Gln Glu Cys Ile Gln 405 410 415  
 Met Lys Ala Arg Leu Thr Gln Glu Leu Gln Ala Lys Asn Met His 420 425 430  
 Asn Val Leu Gln Ala Glu Leu Asp Lys Leu Thr Ser Val Lys Gln Gln 435 440 445  
 Leu Glu Asn Asn Leu Glu Glu Phe Lys Gln Lys Leu Cys Arg Ala Glu 450 455 460  
 Gln Ala Phe Gln Ala Ser Gln Ile Lys Glu Asn Glu Leu Arg Arg Ser 465 470 475 480  
 Met Glu Glu Met Lys Lys Glu Asn Asn Leu Leu Lys Ser His Ser Glu 485 490 495  
 Gln Lys Ala Arg Glu Val Cys His Leu Glu Ala Glu Leu Lys Asn Ile 500 505 510  
 Lys Gln Cys Leu Asn Gln Ser Gln Asn Phe Ala Glu Glu Met Lys Ala 515 520 525  
 Lys Asn Thr Ser Gln Glu Thr Met Leu Arg Asp Leu Gln Glu Lys Ile 530 535 540  
 Asn Gln Gln Asn Ser Leu Thr Leu Glu Lys Leu Lys Leu Ala Val 545 550 555  
 Ala Asp Leu Glu Lys Gln Arg Asp Cys Ser Gln Asp Leu Leu Lys Lys 560 565 570 575  
 Arg Glu His His Ile Glu Gln Leu Asn Asp Lys Leu Ser Lys Thr Glu 580 585 590

580 585 590  
 Lys Glu Ser Lys Ala Leu Leu Ser Ala Leu Glu Leu Lys Lys Lys Glu 595 600 605  
 Tyr Glu Glu Leu Lys Glu Glu Lys Thr Leu Phe Ser Cys Trp Lys Ser 610 615 620  
 Glu Asn Glu Lys Leu Leu Thr Gln Met Glu Ser Glu Lys Glu Asn Leu 625 630 635 640  
 Gln Ser Lys Ile Asn His Leu Glu Thr Cys Leu Lys Thr Gln Gln Ile 645 650 655  
 Lys Ser His Glu Tyr Asn Glu Arg Val Arg Thr Leu Glu Met Asp Arg 660 665 670  
 Glu Asn Leu Ser Val Glu Ile Arg Asn Leu His Asn Val Leu Asp Ser 675 680 685  
 Lys Ser Val Glu Val Glu Thr Gln Lys Leu Ala Tyr Met Glu Leu Gln 690 695 700  
 Gln Lys Ala Glu Phe Ser Asp Gln Lys His Gln Lys Glu Ile Glu Asn 705 710 715 720  
 Met Cys Leu Lys Thr Ser Gln Leu Thr Gly Gln Val Glu Asp Leu Glu 725 730 735  
 His Lys Leu Gln Leu Leu Ser Asn Glu Ile Met Asp Lys Asp Arg Cys 740 745 750  
 Tyr Gln Asp Leu His Ala Glu Tyr Glu Ser Leu Arg Asp Leu Lys Lys 755 760 765  
 Ser Lys Asp Ala Ser Leu Val Thr Asn Glu Asp His Gln Arg Ser Leu 770 775 780  
 Leu Ala Phe Asp Gln Gln Pro Ala Met His His Ser Phe Ala Asn Ile 785 790 795 800  
 Ile Gly Glu Gln Gly Ser Met Pro Ser Glu Arg Ser Glu Cys Arg Leu 805 810 815  
 Glu Ala Asp Gln Ser Pro Lys Asn Ser Ala Ile Leu Gln Asn Arg Val 820 825 830  
 Asp Ser Leu Glu Phe Ser Leu Glu Ser Gln Lys Gln Met Asn Ser Asp 835 840 845  
 Leu Gln Lys Gln Cys Glu Glu Leu Val Gln Ile Lys Gly Glu Ile Glu 850 855 860  
 Glu Asn Leu Met Lys Ala Glu Gln Met His Gln Ser Phe Val Ala Glu 865 870 875 880  
 Thr Ser Gln Arg Ile Ser Lys Leu Gln Glu Asp Thr Ser Ala His Gln 885 890 895

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Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val  
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&lt;213&gt; Homo sapiens

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Lys Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His Val Asn Asp  
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Leu Met Leu Val Lys Leu Asn Ser Gln Ala Arg Leu Ser Ser Met Val  
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Ile Pro Asp Ser Lys Lys Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro  
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215

220

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&lt;213&gt; Homo sapiens

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Glu Ala Ala Arg Ile His Asn His Leu Pro Glu Ile Gln Lys Phe Ser  
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Ser Arg Ile Arg Glu Ala Lys Leu Ala Gly Asp His Ile Glu Tyr Tyr  
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His Lys Thr Tyr Gly Phe His Phe Thr Thr Pro Ala Leu Val Val Glu  
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Lys Asp Ala Val Phe Ile Pro Ala Gly Trp Asp Asn Glu Lys Lys Ile  
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Ala Ile Leu His Glu Asn Phe Thr Thr Val Lys Pro Glu Asp Ala Tyr  
325 330 335  
Glu Asp Phe Ile Val Lys Pro Pro Val Arg Lys Leu Val His Asp Lys  
340 345 350

Glu Leu Ala Ala Glu Asp Glu Gln Val Phe Leu Met Lys Gln Gln Ser  
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Leu Leu Ala Lys Gln pro Ala Thr Pro Thr Arg Ala Ser Glu Ser Pro  
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Ala Arg Gly Pro Ser Gly Ser Pro Arg Thr Gln Gly Arg Gly Pro  
385 390 395

Ala Ser Val pro Ser Ser Ser Pro Gly Thr Ser Val Lys Lys Pro Asp  
405 410 415

Pro Asn Ile Lys Asn Asn Ala Ala Ser Glu Gly Val Leu Ala Ser Phe  
420 425 430

Phe Asn Ser leu leu Ser Lys Lys Thr Gly Ser Pro Gly Ser Pro Gly  
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Ala Gly Gly Val Gln Ser Thr Ala Lys Lys Ser Gly Gln Lys Thr Val  
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Thr Arg Met Arg Ser Arg Thr Ser Ser Phe Thr Glu Gln Leu Asp Glu  
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Gly Thr Pro Asn Arg Glu Ser Gly Asp Thr Gln Ser Phe Ala Gln Lys  
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Leu Gln Leu Arg Val Pro Ser Val Glu Ser Leu Phe Arg Ser Pro Ile  
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Lys Glu Ser leu Phe Arg Ser Ser Ser Lys Glu Ser Leu Val Arg Thr  
85 90 95

Ser Ser Arg Glu Ser Ser Leu Asn Arg Leu Asp Leu Asp Ser Thr Ala  
100 105 110

Ser Phe Asn Pro Pro Ser Asp Met Asp Ser Glu Ala Glu Asp Leu Val  
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Gly Asn Ser Asp Ser Leu Asn Lys Glu Gln Leu Ile Gln Arg Leu Arg  
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Arg Met Glu Arg Ser Leu Ser Ser Tyr Arg Gly Lys Tyr Ser Glu Leu  
155 160 165

Val Thr Ala Tyr Gln Met Leu Gln Arg Glu Lys Lys Lys Leu Gln Gly  
170 175

Ile Leu Ser Gln Ser Gln Asp Lys Ser Leu Arg Arg Ile, Ala Glu Leu  
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Arg Glu Glu Leu Gln Met Asp Gln Gln Ala Lys Lys His Leu Gln Glu  
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Glu Phe Asp Ala Ser Leu Glu Glu Lys Asp Gln Tyr Ile Ser Val Leu  
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Gln Thr Gln Val Ser Leu Leu Lys Gln Arg Leu Arg Asn Gly Pro Met  
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Asn Val Asp Val Leu Lys Pro Leu Pro Gln Leu Glu Pro Gln Ala Glu  
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Val Phe Thr Lys Glu Glu Asn Pro Glu Ser Asp Gly Glu Pro Val Val  
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Glu Asp Gly Thr Ser Val Lys Thr Leu Glu Thr Leu Gln Gln Arg Val  
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Lys Arg Gln Glu Asn Leu Leu Lys Arg Cys Lys Glu Thr Ile Gln Ser  
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His Lys Glu Gln Cys Thr Leu Leu Thr Ser Glu Lys Glu Ala Leu Gln  
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Glu Gln Leu Asp Glu Arg Leu Gln Glu Leu Glu Lys Ile Lys Asp Leu  
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His Met Ala Glu Lys Thr Lys Leu Ile Thr Gln Leu Arg Asp Ala Lys  
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Asn Leu Ile Glu Gln Leu Glu Gln Asp Lys Gly Met Val Ile Ala Glu  
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Thr Lys Arg Gln Met His Glu Thr Leu Glu Met Lys Glu Glu Ile  
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Ala Gln Leu Arg Ser Arg Ile Lys Gln Met Thr Thr Gln Gly Glu Glu  
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Glu Lys Ala Leu Ser Thr Ala Gln Lys Thr Glu Glu Ala Arg Arg Lys  
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Leu Lys Ala Glu Met Asp Glu Gln Ile Lys Thr Ile Glu Lys Thr Ser  
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Glu Glu Glu Arg Ile Ser Leu Gln Gln Glu Leu Ser Arg Val Lys Gln  
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Glu Val Val Asp Val Met Lys Lys Ser Ser Glu Glu Glu Ile Ala Lys 465 470 475  
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 Val Ala Leu Glu Lys Ser Glu Ser Glu Tyr Lys Lys Ile Ser Glu Glu 515 520 525  
 Lys Glu Glu Glu Ser Leu Ala Leu Glu Glu Leu Glu Glu Lys 530 535 540  
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 Glu Lys Ser Leu Glu Glu Aaa Lys Aaa Glu Ser Lys Asp Leu Ala Val 580 585 590  
 His Leu Glu Ala Glu Lys Aaa Lys His Aaa Lys Glu Ile Thr Val Met 595 600 605  
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 Ala Leu Trp Thr Glu Lys Leu Glu Val Leu Lys Glu Glu Tyr Glu Thr 625 630 635  
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 Leu Lys Asp Lys Glu Ile Ile Phe Glu Ala His Ile Glu Glu Met Aaa 660 665 670  
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 Leu Ser Ser Glu Leu Ser Glu Val Leu Lys Ala Arg His Lys Leu Glu 690 695 700  
 Glu Glu Leu Ser Val Leu Lys Asp Glu Thr Asp Lys Met Lys Glu Glu 705 710 715  
 Leu Glu Ala Lys Met Asp Glu Glu Lys Aaa His His Glu Glu Val 725 730 735  
 Asp Ser Ile Ile Lys Glu His Glu Val Ser Ile Glu Arg Thr Glu Lys 740 745 750  
 Ala Leu Lys Asp Glu Ile Aaa Glu Leu Glu Leu Leu Lys Glu Arg 755 760 765  
 Asp Lys His Leu Lys Glu His Glu Ala His Val Glu Aaa Leu Glu Ala 770 775 780

Asp Ile Lys Arg Ser Glu Gly Glu Leu Glu Glu Ala Ser Ala Lys Leu 785 790 795  
 Asp Val Phe Glu Ser Tyr Glu Ser Ala Thr His Glu Glu Thr Lys Ala 805 810 815  
 Tyr Glu Glu Glu Leu Ala Glu Leu Glu Glu Lys Leu Leu Asp Leu Glu 820 825 830  
 Thr Glu Arg Ile Leu Leu Thr Lys Glu Val Ala Glu Val Glu Ala Glu 835 840 845  
 Lys Lys Asp Val Cys Thr Glu Leu Asp Ala His Lys Ile Glu Val Glu 850 855 860  
 Asp Leu Met Glu Glu Leu Glu Lys Glu Aaa Ser Glu Met Glu Glu Lys 865 870 875  
 Val Lys Ser Leu Thr Glu Val Tyr Glu Ser Lys Leu Glu Asp Gly Aaa 885 890 895  
 Lys Glu Glu Glu Glu Thr Lys Glu Ile Leu Val Glu Lys Glu Aaa Met 900 905 910  
 Ile Leu Glu Met Arg Glu Gly Glu Lys Lys Glu Ile Glu Ile Leu Thr 915 920 925  
 Glu Lys Leu Ser Ala Lys Glu Asp Ser Ile His Ile Leu Aaa Glu Glu 930 935 940  
 Tyr Glu Thr Lys Phe Lys Aaa Glu Glu Lys Lys Met Glu Lys Val Lys 945 950 955  
 Glu Lys Ala Lys Glu Met Glu Thr Leu Lys Lys Lys Leu Leu Asp 965 970 975  
 Glu Glu Ala Lys Leu Lys Lys Glu Leu Glu Aaa Thr Ala Leu Glu Leu 980 985 990  
 Ser Glu Lys Glu Lys Glu Phe Aaa Ala Lys Met Leu Glu Met Ala Glu 995 1000 1005  
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 Glu Ala Glu Glu Leu Glu Glu Ile His Glu Ile Glu Leu Glu Glu 1055 1060 1065  
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Glu Leu Lys Met Leu Ala Glu Glu Asp Lys Arg Lys Val Ser Glu 1170  
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Gln Ala Thr His Gln Leu Glu Glu Lys Glu Asn Gln Ile Lys Ser 1305  
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Gln Lys Glu Gly Gly Asn Gln Gln Gln Ala Ala Ser Glu Lys Glu 1335  
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Ala Tyr Glu Lys Asp Glu Gln Ile Asn Leu Leu Lys Glu Glu Leu 1485  
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Val Tyr Ser Met Lys Ala Glu Leu Glu Thr Lys Lys Lys Glu Leu 1605  
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Lys Glu Glu Thr Val Ser Ser His Phe Glu Met Arg Cys Gln Tyr 1765 1770 1775  
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Glu Asp Gln Ser Met Ile Gly His Leu Gln Glu Glu Leu Glu Glu 1795 1800 1805  
Lys Asn Lys Lys Tyr Ser Leu Ile Val Ala Gln His Val Glu Lys 1810 1815 1820  
Glu Gly Gly Lys Asn Asn Ile Gln Ala Lys Gln Asn Leu Glu Asn 1825 1830 1835  
Val Phe Asp Asp Val Gln Lys Thr Leu Gln Glu Lys Glu Leu Thr 1840 1845 1850  
Cys Gln Ile Leu Glu Gln Lys Ile Lys Glu Leu Asp Ser Cys Leu 1855 1860 1865  
Val Arg Gln Lys Glu Val His Arg Val Glu Met Glu Glu Leu Thr 1870 1875 1880  
Ser Lys Tyr Glu Lys Leu Gln Ala Leu Gln Gln Met Asp Gly Arg 1885 1890 1895  
Asn Lys Pro Thr Glu Leu Leu Glu Glu Asn Thr Glu Glu Lys Ser 1900 1905 1910  
Lys Ser His Leu Val Gln Pro Lys Leu Leu Ser Asn Met Glu Ala 1915 1920 1925  
Gln His Asn Asp Leu Glu Phe Lys Leu Ala Gly Ala Glu Arg Glu 1930 1935 1940  
Lys Gln Lys Leu Gly Lys Glu Ile Val Arg Leu Gln Lys Asp Leu 1945 1950 1955  
Arg Met Leu Arg Lys Glu His Gln Gln Glu Leu Glu Ile Leu Lys 1960 1965 1970  
Lys Glu Tyr Asp Gln Glu Arg Glu Glu Lys Ile Lys Gln Glu Gln 1975 1980 1985

Glu Asp Leu Glu Leu Lys His Asn Ser Thr Leu Lys Gln Leu Met 1985 1990 1995  
Arg Glu Phe Asn Thr Gln Leu Ala Gln Lys Glu Gln Glu Leu Glu 2000 2005 2010 2015  
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Tyr Glu Glu Ile Leu Asp Ala Arg Glu Glu Glu Met Thr Ala Lys 2065 2070 2075  
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His Asn Leu Glu Asp Arg Leu Lys Lys Tyr Glu Lys Asn Val Tyr 2140 2145 2150  
Ala Thr Thr Val Gly Thr Pro Tyr Lys Gly Gly Asn Leu Tyr His 2155 2160 2165  
Thr Asp Val Ser Leu Phe Gly Glu Pro Thr Glu Phe Glu Tyr Leu 2170 2175 2180  
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Lys Ser Met Gln Asp Arg Leu Arg Leu Gly His Phe Thr Thr Val Arg  
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His Gly Ala Ser Phe Thr Glu Gln Trp-Thr Asp Gly Tyr Ala Phe Gln  
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Gln Ala Pro Pro Ala Thr Asn Glu Gln Lys Gln Arg Lys Ser Lys Thr

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Glu Ile Gln Ala Glu Leu Glu Arg Leu Glu Arg Val Arg Asn Leu His  
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Asp His Pro Thr Leu Asn Asp Arg Tyr Leu Leu His Leu Leu Gly  
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His Lys Glu Leu Asp His Pro Arg Ile Val Lys Leu Tyr Asp Tyr Phe  
465 470 475 480  
Ser Leu Asp Thr Asp Ser Phe Cys Thr Val Leu Glu Tyr Cys Glu Gly  
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Glu Ala Arg Ser Ile Ile Met Gln Ile Val Asn Ala Leu Lys Tyr Leu  
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Phe Gly Leu Ser Lys Ile Met Asp Asp Ser Tyr Asn Ser Val Asp  
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Gly Met Glu Leu Thr Ser Gln Gly Ala Gly Thr Trp Tyr Leu Pro  
580 585 590  
Pro Glu Cys Phe Val Val Gly Lys Glu Pro Pro Lys Ile Ser Asn Lys  
595 600 605  
Val Asp Val Trp Ser Val Gly Val Ile Phe Tyr Gln Cys Leu Tyr Gly  
610 615 620  
Arg Lys Pro Phe Gly His Asn Gln Ser Gln Asp Ile Leu Gln Glu  
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Asn Thr Ile Leu Lys Ala Thr Glu Val Gln Phe Pro Pro Lys Pro Val 655  
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Val Thr Pro Glu Ala Lys Ala Phe Ile Arg Arg Cys Leu Ala Tyr Arg 670  
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Lys Lys Arg His Glu Met Pro Pro His Ile Tyr Ala Ile Ser Glu Ser 160  
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Ala Tyr Arg Cys Met Leu Gln Asp Arg Glu Asp Gln Ser Ile Leu Cys 175  
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Thr Gly Glu Ser Gly Ala Gly Lys Thr Glu Asn Thr Lys Lys Val Ile 190  
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Gln Tyr Leu Ala His Val Ala Ser Ser His Lys Gly Arg Lys Asp His 205  
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Asn Ile Pro Gly Glu Leu Glu Arg Gln Leu Leu Gln Ala Asn Pro Ile 220  
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Arg Gln Ala Lys Asp Glu Arg Thr Phe His Ile Phe Tyr Gln Leu Leu 285  
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Ser Gly Ala Gly Glu His Leu Lys Ser Asp Leu Leu Leu Glu Gly Phe 300  
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Gln Asp Lys Asp Asn Phe Gln Glu Thr Met Glu Ala Met His Ile Met 335  
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Gly Phe Ser His Glu Glu Ile Leu Ser Met Leu Lys Val Val Ser Ser 350  
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Val Leu Gln Phe Gly Asn Ile Ser Phe Lys Lys Glu Arg Asn Thr Asp 365  
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Gln Ala Ser Met Pro Glu Asn Thr Val Ala Gln Lys Leu Cys His Leu 380  
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Leu Gly Met Asn Val Met Glu Phe Thr Arg Ala Ile Leu Thr Pro Arg 400  
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Ile Lys Val Gly Arg Asp Tyr Val Gln Lys Ala Gln Thr Lys Glu Gln 415  
405  
Ala Asp Phe Ala Val Glu Ala Leu Ala Lys Ala Thr Tyr Glu Arg Leu 430  
420  
Phe Arg Trp Leu Val His Arg Ile Asn Lys Ala Leu Asp Arg Thr Lys 445  
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Arg Gln Gly Ala Ser Phe Ile Gly Ile Leu Asp Ile Ala Gly Phe Glu 460  
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Ile Phe Glu Leu Asn Ser Phe Glu Gln Leu Cys Ile Asn Tyr Thr Asn 480  
465  
Glu Lys Leu Gln Gln Leu Phe Asn His Thr Met Phe Ile Leu Glu Gln 495  
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Pro Gly Val Leu Ala Leu Leu Asp Glu Glu Cys Trp Phe Pro Lys Ala  
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Thr Asp Lys Thr Phe Val Glu Lys Leu Val Gln Glu Gln Gly Ser His  
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Ser Lys Phe Gln Lys Pro Arg Gln Leu Lys Asp Lys Ala Asp Phe Cys  
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Ile Ile His Tyr Ala Gly Lys Val Asp Tyr Lys Ala Asp Glu Trp Leu  
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Met Lys Asn Met Asp Pro Leu Asn Asp Asn Val Ala Thr Leu Leu His  
595 600 605

Gln Ser Ser Asp Arg Phe Val Ala Glu Leu Trp Lys Asp Val Asp Arg  
610 615 620

Ile Val Gly Leu Asp Gln Val Thr Gly Met Thr Glu Thr Ala Phe Gly  
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Ser Ala Tyr Lys Thr Lys Lys Gly Met Phe Arg Thr Val Gly Gln Leu  
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Tyr Lys Glu Ser Leu Thr Lys Leu Met Ala Thr Leu Arg Asn Thr Asn  
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Pro Asn Phe Val Arg Cys Ile Ile Pro Asn His Glu Lys Arg Ala Gly  
675 680 685

Lys Leu Asp Pro His Leu Val Leu Asp Gln Leu Arg Cys Asn Gly Val  
690 695 700

Leu Glu Gly Ile Arg Ile Cys Arg Gln Gly Phe Pro Asn Arg Ile Val  
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Phe Gln Glu Phe Arg Gln Arg Tyr Glu Ile Leu Thr Pro Asn Ala Ile  
725 730 735

Pro Lys Gly Phe Met Asp Gly Lys Gln Ala Cys Glu Arg Met Ile Arg  
740 745 750

Ala Leu Glu Leu Asp Pro Asn Leu Tyr Arg Ile Gly Gln Ser Lys Ile  
755 760 765

Phe Arg Ala Gly Val Leu Ala His Leu Glu Glu-Glu Arg Asp Leu  
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Lys Ile Thr Asp Ile Ile Ile Phe Phe Gln Ala Val Cys Arg Gly Cys  
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Leu Ala Arg Lys Ala Phe Ala Lys Lys Gln Gln Gln Leu Ser Ala Leu  
805 810 815

Lys Val Leu Gln Arg Asn Cys Ala Ala Tyr Leu Lys Leu Arg His Trp  
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Gln Trp Trp Arg Val Phe Thr Lys Val Lys Pro Leu Leu Gln Val Thr  
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850 855 860

Lys Glu Lys Gln Thr Lys Val Glu Gly Glu Leu Glu Met Glu Arg  
865 870 875 880

Lys His Gln Gln Leu Leu Glu Glu Lys Asn Ile Leu Ala Glu Gln Leu  
885 890 895

Gln Ala Glu Thr Glu Leu Phe Ala Glu Ala Glu Glu Met Arg Ala Arg  
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Leu Ala Ala Lys Lys Gln Glu Leu Glu Glu Ile Leu His Asp Leu Glu  
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Ser Arg Val Glu Glu Glu Glu Arg Asn Gln Ile Leu Gln Asn Glu  
930 935 940

Lys Lys Lys Met Gln Ala His Ile Gln Asp Leu Glu Glu Gln Leu Asp  
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Glu Glu Glu Gly Ala Arg Gln Lys Leu Gln Leu Glu Lys Val Thr Ala  
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Gln Asn Ser Lys Phe Ile Lys Glu Lys Lys Leu Met Glu Asp Arg Ile  
995 1000 1005

Ala Glu Cys Ser Ser Gln Leu Ala Glu Glu Glu Lys Ala Lys  
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Asn Leu Ala Lys Ile Arg Asn Lys Gln Glu Val Met Ile Ser Asp  
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Glu Lys Ala Lys Arg Lys Leu Asp Gly Glu Thr Thr Asp Leu Gln  
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Asp Gln Ile Ala Glu Leu Gln Ala Gln Ile Asp Glu Leu Lys Leu  
1070 1075 1080

Gln Leu Ala Lys Lys Glu Glu Glu Leu Gln Gly Ala Leu Ala Arg  
1085 1090 1095

Gly Asp Asp Glu Thr Leu His Lys Asn Asn Ala Leu Lys Val Val  
1100 1105 1110

Arg Glu Leu Gln Ala Gln Ile Ala Glu Leu Gln Glu Asp Phe Glu  
1115 1120 1125

Ser Glu Lys Ala Ser Arg Asn Lys Ala Glu Lys Gln Lys Arg Asp  
1130 1135 1140

Leu Ser Glu Glu Leu Glu Ala Leu Lys Thr Glu Leu Glu Asp Thr  
1145 1150 1155



1143                    1150                    1155  
Leu Asp   Thr Thr Ala Ala Gln   Gln Glu Leu Arg Thr   Lys Arg Glu  
1160                    1163  
Gln Glu   Val Ala Glu Leu Lys   Lys Ala Glu Glu   Glu Thr Lys  
1175                    1180                    1185  
Asn His   Glu Ala Gln Ile Gln   Asp Met Arg Gln Arg   His Ala Thr  
1190                    1195                    1200  
Ala Leu   Glu Glu Leu Ser Glu   Gln Leu Glu Gln Ala   Lys Arg Phe  
1205                    1210                    1215  
Lys Ala   Asn Leu Glu Lys Asn   Lys Gln Gly Leu Glu   Thr Asp Asn  
1220                    1225                    1230  
Lys Glu   Leu Ala Cys Glu Val   Lys Val Leu Gln Gln   Val Lys Ala  
1235                    1240                    1245  
Glu Ser   Glu His Lys Arg Lys   Lys Leu Asp Ala Gln   Val Gln Glu  
1250                    1255                    1260  
Leu His   Ala Lys Val Ser Glu   Gly Asp Arg Leu Arg   Val Glu Leu  
1265                    1270                    1275  
Ala Glu   Lys Ala Ser Lys Leu   Gln Asn Leu Asp Asn   Val Ser  
1280                    1285                    1290  
Thr Leu   Leu Glu Glu Ala Glu   Lys Lys Gly Ile Lys   Phe Ala Lys  
1295                    1300                    1305  
Asp Ala   Ala Ser Leu Glu Ser   Gln Leu Gln Asp Thr   Gln Glu Leu  
1310                    1315                    1320  
Leu Gln   Glu Glu Thr Arg Gln   Lys Leu Asn Leu Ser   Ser Arg Ile  
1325                    1330                    1335  
Arg Gln   Leu Glu Glu Glu Lys   Asn Ser Leu Gln Glu   Gln Gln Glu  
1340                    1345                    1350  
Glu Glu   Glu Glu Ala Arg Lys   Asn Leu Glu Lys Gln   Val Leu Ala  
1355                    1360                    1365  
Leu Gln   Ser Gln Leu Ala Asp   Thr Lys Lys Lys Val   Asp Asp Asp  
1370                    1375                    1380  
Leu Gly   Thr Ile Glu Ser Leu   Glu Glu Ala Lys Lys   Lys Leu Leu  
1385                    1390                    1395  
Lys Asp   Ala Glu Ala Leu Ser   Gln Arg Leu Glu Glu   Lys Ala Leu  
1400                    1405                    1410  
Ala Tyr   Asp Lys Leu Glu Lys   Thr Lys Asn Arg Leu   Gln Gln Glu  
1415                    1420                    1425  
Leu Asp   Asp Leu Thr Val Asp   Leu Asp His Gln Arg   Gln Val Ala  
1430                    1435                    1440

Ser Asn   Leu Glu Lys Lys Gln   Lys Lys Phe Asp Gln   Leu Leu Ala  
1445                    1450                    1455  
Glu Glu   Lys Ser Ile Ser Ala   Arg Tyr Ala Glu Glu   Arg Asp Arg  
1460                    1465                    1470  
Ala Glu   Ala Glu Ala Arg Glu   Lys Glu Thr Lys Ala   Leu Ser Leu  
1475                    1480                    1485  
Ala Arg   Ala Leu Glu Glu Ala   Leu Glu Ala Lys Glu   Glu Phe Glu  
1490                    1495                    1500  
Arg Gln   Asn Lys Gln Leu Arg   Ala Asp Met Glu Asp   Leu Met Ser  
1505                    1510                    1515  
Ser Lys   Asp Asp Val Gly Lys   Asn Val His Glu Leu   Glu Lys Ser  
1520                    1525                    1530  
Lys Arg   Ala Leu Glu Gln Gln   Val Glu Glu Met Arg   Thr Gln Leu  
1535                    1540                    1545  
Glu Glu   Leu Glu Asp Glu Leu   Gln Ala Thr Glu Asp   Ala Lys Leu  
1550                    1555                    1560  
Arg Leu   Glu Val Asn Met Gln   Ala Met Lys Ala Gln   Phe Glu Arg  
1565                    1570                    1575  
Asp Leu   Gln Thr Arg Asp Glu   Gln Asn Glu Glu Lys   Lys Arg Leu  
1580                    1585                    1590  
Leu Ile   Lys Gln Val Arg Glu   Leu Glu Ala Glu Leu   Glu Asp Glu  
1595                    1600                    1605  
Arg Lys   Gln Arg Ala Leu Ala   Val Ala Ser Lys Lys   Lys Met Glu  
1610                    1615                    1620  
Ile Asp   Leu Lys Asp Leu Glu   Ala Gln Ile Glu Ala   Ala Asn Lys  
1625                    1630                    1635  
Ala Arg   Asp Glu Val Ile Lys   Gln Leu Arg Lys Leu   Gln Ala Gln  
1640                    1645                    1650  
Met Lys   Asp Tyr Gln Arg Glu   Leu Glu Glu Ala Arg   Ala Ser Arg  
1655                    1660                    1665  
Asp Glu   Ile Phe Ala Gln Ser   Lys Glu Ser Glu Lys   Lys Leu Lys  
1670                    1675                    1680  
Ser Leu   Glu Ala Glu Ile Leu   Gln Leu Gln Glu Glu   Leu Ala Ser  
1685                    1690                    1695  
Ser Glu   Arg Ala Arg Arg His   Ala Glu Gln Glu Arg   Asp Glu Leu  
1700                    1705                    1710  
Ala Asp   Glu Ile Thr Asn Ser   Ala Ser Gly Lys Ser   Ala Leu Leu  
1715                    1720                    1725  
Asp Glu   Lys Arg Arg Leu Glu   Ala Arg Ile Ala Gln   Leu Glu Glu  
1730                    1735                    1740

Glu Leu Glu Glu Glu Ser Asn Met Glu Leu Leu Asn Asp Arg  
1745 1750 1755  
Phe Arg Lys Thr Thr Leu Glu Val Asp Thr Leu Asn Ala Glu Leu  
1760 1765 1770  
Ala Ala Glu Arg Ser Ala Ala Gln Lys Ser Asp Asn Ala Arg Gln  
1775 1780 1785  
Gln Leu Glu Arg Gln Asn Lys Glu Leu Lys Ala Lys Leu Gln Glu  
1790 1795 1800  
Leu Glu Gly Ala Val Lys Ser Lys Phe Lys Ala Thr Ile Ser Ala  
1805 1810 1815  
Leu Glu Ala Lys Ile Gly Gln Leu Glu Glu Gln Leu Glu Gln Glu  
1820 1825 1830  
Ala Lys Glu Arg Ala Ala Ala Asn Lys Leu Val Arg Arg Thr Glu  
1835 1840 1845  
Lys Lys Leu Lys Glu Ile Phe Met Gln Val Glu Asp Glu Arg Arg  
1850 1855 1860  
His Ala Asp Gln Tyr Lys Glu Gln Met Glu Lys Ala Asn Ala Arg  
1865 1870 1875  
Met Lys Gln Leu Lys Arg Glu Leu Glu Glu Ala Glu Glu Ala  
1880 1885 1890  
Thr Arg Ala Asn Ala Ser Arg Arg Lys Leu Gln Arg Glu Leu Asp  
1895 1900 1905  
Asp Ala Thr Glu Ala Asn Glu Gly Leu Ser Arg Glu Val Ser Thr  
1910 1915 1920  
Leu Lys Asn Arg Leu Arg Arg Gly Gly Pro Ile Ser Phe Ser Ser  
1925 1930 1935  
Ser Arg Ser Gly Arg Arg Gln Leu His Leu Glu Gly Ala Ser Leu  
1940 1945 1950  
Glu Leu Ser Asp Asp Thr Glu Ser Lys Thr Ser Asp Val Asn  
1955 1960 1965  
Glu Thr Gln Pro Gln Ser Glu  
1970 1975  
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Ile Gln Asp Ala Ala Ser Lys Asn Glu Asp Gln Glu Met Cys His Glu  
20 25 30

Phe Gln Ala Phe Met Lys Asn Gly Lys Leu Phe Cys Pro Gln Asp Lys  
35 40 45  
Lys Phe Phe Gln Ser Leu Asp Gly Ile Met Phe Ile Asn Lys Cys Ala  
50 55 60  
Thr Cys Lys Met Ile Leu Glu Lys Glu Ala Lys Ser Gln Lys Arg Ala  
65 70 75 80  
Arg His Leu Ala Arg Ala Pro Lys Ala Thr Ala Pro Thr Glu Leu Asn  
85 90 95  
Cys Asp Asp Phe Lys Lys Gly Glu Arg Asp Gly Asp Phe Ile Cys Pro  
100 105 110  
Asp Tyr Tyr Glu Ala Val Cys Gly Thr Asp Gly Lys Thr Tyr Asp Asn  
115 120 125  
Arg Cys Ala Leu Cys Ala Glu Asn Ala Lys Thr Gly Ser Gln Ile Gly  
130 135 140  
Val Lys Ser Glu Gly Glu Cys Lys Ser Ser Asn Pro Glu Gln Asp Val  
145 150 155  
Cys Ser Ala Phe Arg Pro Phe Val Arg Asp Gly Arg Leu Gly Cys Thr  
160 165 170 175  
Arg Glu Asn Asp Pro Val Leu Gly Pro Asp Gly Lys Thr His Gly Asn  
180 185 190  
Lys Cys Ala Met Cys Ala Glu Leu Phe Leu Lys Glu Ala Glu Asn Ala  
195 200 205  
Lys Arg Gln Gly Glu Thr Arg Ile Arg Arg Asn Ala Glu Lys Asp Phe  
210 215 220  
Cys Lys Glu Tyr Glu Lys Lys Gln Val Arg Asn Gly Arg Leu Phe Cys Thr  
225 230 235  
Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly Arg Met His Gly Asn  
240 245 250 255  
Lys Cys Ala Leu Cys Ala Glu Ile Phe Lys Arg Arg Phe Ser Glu Glu  
260 265 270  
Asn Ser Lys Thr Asp Gln Asn Leu Gly Lys Ala Glu Glu Lys Thr Lys  
275 280 285  
Val Lys Arg Glu Ile Val Lys Leu Cys Ser Gln Tyr Gln Asn Gln Ala  
290 295 300  
Lys Asn Gly Ile Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Arg Gly  
305 310 315 320  
Pro Asp Gly Lys Met His Gly Asn Leu Cys Ser Met Cys Gln Val Tyr  
325 330 335  
Phe Gln Ala Glu Asn Glu Lys Lys Lys Ala Glu Ala Arg Ala Arg  
340 345 350

Asn Lys Arg Glu Ser Gly Lys Ala Thr Ser Tyr Ala Glu Leu Cys Asn 365  
355 360  
Glu Tyr Arg Lys Leu Val Arg Asn Gly Lys Leu Ala Cys Thr Arg Glu 380  
370 375  
Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys Val His Gly Asn Thr Cys 400  
385 390 395  
Ser Met Cys Glu Val Phe Phe Gln Ala Glu Glu Glu Lys Lys 415  
405 410  
Lys Glu Gly Glu Ser Arg Asn Lys Arg Gln Ser Lys Ser Thr Ala Ser 430  
420 425  
Phe Glu Glu Leu Cys Ser Glu Tyr Arg Lys Ser Arg Lys Asn Gly Arg 445  
435 440  
Leu Phe Cys Thr Arg Glu Asn Asp Pro Ile Gln Gly Pro Asp Gly Lys 460  
450 455  
Met His Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln Gln Glu 480  
465 470 475  
Glu Arg Ala Arg Ala Lys Ala Lys Arg Glu Ala Ala Lys Glu Ile Cys 495  
485 490  
Ser Glu Phe Arg Asp Gln Val Arg Asn Gly Thr Leu Ile Cys Thr Arg 510  
500 505  
Glu His Asn Pro Val Arg Gly Pro Asp Gly Lys Met His Gly Asn Lys 525  
515 520  
Cys Ala Met Cys Ala Ser Val Phe Lys Leu Glu Glu Glu Lys Lys 540  
530 535  
Asn Asp Lys Glu Glu Lys Gly Lys Val Glu Ala Glu Lys Val Lys Arg 560  
545 550 555  
Glu Ala Val Gln Glu Leu Cys Ser Glu Tyr Arg His Tyr Val Arg Asn 575  
565 570  
Gly Arg Leu Pro Cys Thr Arg Glu Asn Asp Pro Ile Glu Gly Leu Asp 590  
580 585  
Gly Lys Ile His Gly Asn Thr Cys Ser Met Cys Glu Ala Phe Phe Gln 605  
595 600  
Gln Glu Ala Lys Glu Lys Glu Arg Ala Glu Pro Arg Ala Lys Val Lys 620  
610 615  
Arg Glu Ala Glu Lys Glu Thr Cys Asp Glu Phe Arg Arg Leu Leu Gln 640  
625 630 635  
Asn Gly Lys Leu Phe Cys Thr Arg Glu Asn Asp Pro Val Arg Gly Pro 655  
645 650  
Asp Gly Lys Thr His Gly Asn Lys Cys Ala Met Cys Lys Ala Val Phe

660 665 670  
Gln Lys Glu Asn Glu Arg Lys Arg Lys Glu Glu Asp Gln Arg 685  
675 680  
Asn Ala Ala Gly His Gly Ser Ser Gly Gly Gly Gly Asn Thr Gln 700  
690 695  
Asp Glu Cys Ala Glu Tyr Gln Gln Met Lys Asn Gly Arg Leu Ser 720  
705 710 715  
Cys Thr Arg Glu Ser Asp Pro Val Arg Asp Ala Asp Gly Lys Ser Tyr 735  
725 730  
Asn Asn Gln Cys Thr Met Cys Lys Ala Lys Leu Glu Arg Glu Ala Glu 750  
740 745  
Arg Lys Asn Glu Tyr Ser Arg Ser Arg Ser Asn Gly Thr Gly Ser Glu 765  
755 760  
Ser Gly Lys Asp Thr Cys Asp Glu Phe Arg Ser Gln Met Lys Asn Gly 780  
770 775  
Lys Leu Ile Cys Thr Arg Glu Ser Asp Pro Val Arg Gly Pro Asp Gly 800  
785 790 795  
Lys Thr His Gly Asn Lys Cys Thr Met Cys Lys Glu Lys Leu Glu Arg 815  
805 810  
Glu Ala Ala Glu Lys Lys Lys Glu Asp Glu Asp Arg Ser Asn Thr 830  
820 825  
Gly Glu Arg Ser Asn Thr Gly Glu Arg Ser Asn Asp Lys Glu Asp Leu 845  
835 840  
Cys Arg Glu Phe Arg Ser Met Gln Arg Asn Gly Lys Leu Ile Cys Thr 860  
850 855  
Arg Glu Asn Asn Pro Val Arg Gly Pro Tyr Gly Lys Met His Ile Asn 880  
865 870 875  
Lys Cys Ala Met Cys Gln Ser Ile Phe Asp Arg Glu Ala Asn Glu Arg 895  
885 890  
Lys Lys Lys Asp Glu Glu Lys Ser Ser Ser Lys Pro Ser Asn Asn Ala 910  
900 905  
Lys Asp Glu Cys Ser Glu Phe Arg Asn Tyr Ile Arg Asn Asn Glu Leu 925  
915 920  
Ile Cys Pro Arg Glu Asn Asp Pro Val His Gly Ala Asp Gly Lys Phe 940  
930 935  
Tyr Thr Asn Lys Cys Tyr Met Cys Arg Ala Val Phe Leu Thr Glu Ala 960  
945 950 955  
Leu Glu Arg Ala Lys Leu Gln Glu Lys Pro Ser His Val Arg Ala Ser 975  
965 970

Gln Glu Asp Ser Pro Asp Ser Phe Ser Ser Leu Asp Ser Glu Met  
985 990

Cys Lys Asp Tyr Arg Val Leu Pro Arg Ile Gly Tyr Leu Cys Pro Lys  
995 1000 1005

Asp Leu Lys Pro Val Cys Gly Asp Asp Gly Gln Thr Tyr Asn Asn  
1010 1015 1020

Pro Cys Met Leu Cys His Glu Asn Leu Ile Arg Gln Thr Asn Thr  
1025 1030 1035

His Ile Arg Ser Thr Gly Lys Cys Glu Glu Ser Ser Thr Pro Gly  
1040 1045 1050

Thr Thr Ala Ala Ser Met Pro Pro Ser Asp Glu  
1055 1060

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<211> 125  
<212> PRT  
<213> Homo sapiens  
<400> 159

Met His Lys Glu Glu His Glu Val Ala Val Leu Gly Ala Pro Pro Ser  
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Thr Ile Leu Pro Arg Ser Thr Val Ile Asn Ile His Ser Glu Thr Ser  
20 25 30

Val Pro Asp His Val Val Trp Ser Leu Phe Asn Thr Leu Phe Leu Asn  
35 40 45

Trp Cys Cys Leu Gly Phe Ile Ala Phe Ala Tyr Ser Val Lys Ser Arg  
50 55 60

Asp Arg Lys Met Val Gly Asp Val Thr Gly Ala Gln Ala Tyr Ala Ser  
65 70 75 80

Thr Ala Lys Cys Leu Asn Ile Trp Ala Leu Ile Leu Gly Ile Leu Met  
85 90 95

Thr Ile Gly Phe Ile Leu Leu Leu Val Phe Gly Ser Val Thr Val Tyr  
100 105 110

His Ile Met Leu Gln Ile Ile Gln Glu Lys Arg Gly Tyr  
115 120 125

<210> 160  
<211> 400  
<212> PRT  
<213> Homo sapiens  
<400> 160

Met Met Asp Leu Arg Asn Thr Pro Ala Lys Ser Leu Asp Lys Phe Ile  
1 5 10 15

Glu Asp Tyr Leu Leu Pro Asp Thr Cys Phe Arg Met Gln Ile Asp His  
20 25 30

Ala Ile Asp Ile Ile Cys Gly Phe Leu Lys Glu Arg Cys Phe Arg Gly

35 40 45

Ser Ser Tyr Pro Val Cys Val Ser Lys Val Val Lys Gly Gly Ser Ser  
50 55 60

Gly Lys Gly Thr Thr Leu Arg Gly Arg Ser Asp Ala Asp Leu Val Val  
65 70 75 80

Phe Leu Ser Pro Leu Thr Thr Phe Gln Asp Gln Leu Asn Arg Arg Gly  
85 90 95

Glu Phe Ile Gln Glu Ile Arg Arg Gln Leu Glu Ala Cys Gln Arg Glu  
100 105 110

Arg Ala Leu Ser Val Lys Phe Glu Val Gln Ala Pro Arg Trp Gly Asn  
115 120 125

Pro Arg Ala Leu Ser Phe Val Leu Ser Ser Leu Gln Leu Gly Glu Gly  
130 135 140

Val Glu Phe Asp Val Leu Pro Ala Phe Asp Ala Leu Gly Gln Leu Thr  
145 150 155 160

Gly Ser Tyr Lys Pro Asn Pro Gln Ile Tyr Val Lys Leu Ile Glu Glu  
165 170 175

Cys Thr Asp Leu Gln Lys Glu Gly Phe Ser Thr Cys Phe Thr Glu  
180 185 190

Leu Gln Arg Asp Phe Leu Lys Gln Arg Pro Thr Lys Leu Lys Ser Leu  
195 200 205

Ile Arg Leu Val Lys His Trp Tyr Gln Asn Cys Lys Lys Leu Gly  
210 215 220

Lys Leu Pro Pro Gln Tyr Ala Leu Glu Leu Leu Thr Val Tyr Ala Trp  
225 230 235 240

Glu Arg Gly Ser Met Lys Thr His Phe Asn Thr Ala Gln Gly Phe Arg  
245 250 255

Thr Val Leu Glu Leu Val Ile Asn Tyr Gln Gln Leu Cys Ile Tyr Trp  
260 265 270

Thr Lys Tyr Tyr Asp Phe Lys Asn Pro Ile Ile Glu Lys Tyr Leu Arg  
275 280 285

Arg Gln Leu Thr Lys Pro Arg Pro Val Ile Leu Asp Pro Ala Asp Pro  
290 295 300

Thr Gly Asn Leu Gly Gly Asp Pro Lys Gly Trp Arg Gln Leu Ala  
305 310 315 320

Gln Glu Ala Glu Ala Trp Leu Asn Tyr Pro Cys Phe Lys Asn Trp Asp  
325 330 335

Gly Ser Pro Val Ser Ser Trp Ile Leu Leu Ala Glu Ser Asn Ser Thr  
340 345 350

Asp Asp Glu Thr Asp Asp Pro Arg Thr Tyr Gln Lys Tyr Gly Tyr Ile  
355 360 365  
Gly Thr His Glu Tyr Pro His Phe Ser His Arg Pro Ser Thr Leu Gln  
370 375 380  
Ala Ala Ser Thr Pro Gln Ala Glu Glu Asp Thr Cys Thr Ile Leu  
385 390 395 400  
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Met Glu Asn Gln Val Leu Thr Pro His Val Tyr Trp Ala Gln Arg His  
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Arg Glu Leu Tyr Arg Val Glu Leu Ser Asp Val Gln Asn Pro Ala  
20 25 30  
Ile Ser Ile Thr Glu Asn Val Leu His Phe Lys Ala Gln Gly His Gly  
35 40 45  
Ala Lys Gly Asp Asn Val Tyr Glu Phe His Leu Glu Phe Leu Asp Leu  
50 55 60  
Val Lys Pro Glu Pro Val Tyr Lys Leu Thr Gln Arg Gln Val Asn Ile  
65 70 75 80  
Thr Val Gln Lys Lys Val Ser Gln Trp Trp Glu Arg Leu Thr Lys Gln  
85 90 95  
Glu Lys Arg Pro Leu Phe Leu Ala Pro Asp Phe Asp Arg Trp Leu Asp  
100 105 110  
Glu Ser Asp Ala Glu Met Glu Leu Arg Ala Lys Glu Glu Glu Arg Leu  
115 120 125  
Asn Lys Leu Arg Leu Glu Ser Glu Gly Ser Pro Glu Thr Leu Thr Asn  
130 135 140  
Leu Arg Lys Gly Tyr Leu Phe Met Tyr Asn Leu Val Gln Phe Leu Gly  
145 150 155 160  
Phe Ser Trp Ile Phe Val Asn Leu Thr Val Arg Phe Cys Ile Leu Gly  
165 170 175  
Lys Glu Ser Phe Tyr Asp Thr Phe His Thr Val Ala Asp Met Met Tyr  
180 185 190  
Phe Cys Gln Met Leu Ala Val Glu Thr Ile Asn Ala Ala Ile Gly  
195 200 205  
Val Thr Thr Ser Pro Val Leu Pro Ser Leu Ile Gln Leu Leu Gly Arg  
210 215 220  
Asn Phe Ile Leu Phe Ile Phe Gly Thr Met Glu Glu Met Gln Asn  
225 230 235 240

Lys Ala Val Val Phe Phe Val Phe Tyr Leu Trp Ser Ala Ile Glu Ile.  
245 250 255  
Phe Arg Tyr Ser Phe Tyr Met Leu Thr Cys Ile Asp Met Asp Trp Lys  
260 265 270  
Val Leu Thr Trp Leu Arg Tyr Thr Leu Trp Ile Pro Leu Tyr Pro Leu  
275 280 285  
Gly Cys Leu Ala Glu Ala Val Ser Val Ile Gln Ser Ile Pro Ile Phe  
290 295 300  
Asn Glu Thr Gly Arg Phe Ser Phe Thr Leu Pro Tyr Pro Val Lys Ile  
305 310 315 320  
Lys Val Arg Phe Ser Phe Phe Leu Gln Ile Tyr Leu Ile Met Ile Phe  
325 330 335  
Leu Gly Leu Tyr Ile Asn Phe Arg His Leu Tyr Lys Gln Arg Arg Leu  
340 345 350  
Lys Met Arg Ala Gly Ala Val Ala His Ala Cys Asp Pro Ser Ala Leu  
355 360 365  
Gly Gly  
370  
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<211> 372  
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<213> Homo sapiens  
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Met Leu Asp Gly Leu Gly Val Val Ala Ile Ser Ile Phe Gly Ile Gln  
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Leu Lys Thr Glu Gly Ser Leu Arg Thr Ala Val Pro Gly Ile Pro Thr  
20 25 30  
Gln Ser Ala Phe Asn Lys Cys Leu Gln Arg Tyr Ile Gly Ala Leu Gly  
35 40 45  
Ala Arg Val Ile Cys Asp Asn Ile Pro Gly Leu Val Ser Arg Gln Arg  
50 55 60  
Gln Leu Cys Gln Arg Tyr Pro Asp Ile Met Arg Ser Val Gly Glu Gly  
65 70 75 80  
Ala Arg Glu Trp Ile Arg Glu Cys Gln His Gln Phe Arg His His Arg  
85 90 95  
Trp Asn Cys Thr Thr Leu Asp Arg Asp His Thr Val Phe Gly Arg Val  
100 105 110  
Met Leu Arg Ser Ser Arg Glu Ala Ala Phe Val Tyr Ala Ile Ser Ser  
115 120 125  
Ala Gly Val Ile His Ala Ile Thr Arg Ala Cys Ser Gln Gly Glu Leu  
130 135 140

Ser Val Cys Ser Cys Asp Pro Tyr Thr Arg Gly Arg His His Asp Gln  
145 130 135  
Arg Gly Thr Phe Asp Trp Gly Cys Ser Asp Asn Ile His Tyr Gly  
165 170 175  
Val Arg Phe Ala Lys Ala Phe Val Asp Ala Lys Glu Lys Arg Leu Lys  
180 185 190  
Asp Ala Arg Ala Leu Met Asn Leu His Asn Asn Arg Cys Gly Arg Thr  
195 200 205  
Ala Val Arg Arg Phe Val Lys Leu Glu Cys Lys Cys His Gly Val Ser  
210 215 220  
Gly Ser Cys Thr Leu Arg Thr Cys Trp Arg Ala Leu Ser Asp Phe Arg  
225 230 235  
Arg Thr Gly Asp Tyr Leu Arg Arg Arg Tyr Asp Gly Ala Val Gln Val  
245 250 255  
Met Ala Thr Gln Asp Gly Ala Asn Phe Thr Ala Ala Arg Gln Gly Tyr  
260 265 270  
Arg Arg Ala Thr Arg Ser Asp Leu Val Tyr Phe Asp Asn Ser Pro Asp  
275 280 285  
Tyr Cys Val Leu Asp Lys Ala Ala Gly Ser Leu Gly Thr Ala Gly Arg  
290 295 300  
Val Cys Ser Lys Thr Ser Lys Gly Thr Asp Gly Cys Glu Ile Met Cys  
305 310 315  
Cys Gly Arg Gly Tyr Asp Thr Thr Arg Val Thr Arg Val Thr Gln Cys  
325 330 335  
Glu Cys Lys Phe His Trp Cys Cys Ala Val Arg Cys Lys Glu Cys Arg  
340 345 350  
Asn Thr Val Asp Val His Thr Cys Lys Ala Pro Lys Lys Ala Glu Trp  
355 360 365  
Leu Asp Gln Thr  
370  
<210> 163  
<211> 249  
<212> PRT  
<213> Homo sapiens  
<400> 163  
Met Lys Leu Asn Ile Ser Phe Pro Ala Thr Gly Cys Gln Lys Leu Ile  
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Glu Val Asp Asp Glu Arg Thr Leu Arg Thr Phe Tyr Glu Lys Arg Met  
20 25 30  
Ala Thr Glu Val Ala Ala Asp Ala Leu Glu Glu Trp Lys Gly Tyr  
35 40 45

Val Val Arg Ile Ser Gly Asn Asp Lys Gln Gly Phe Pro Met Lys  
50 55 60  
Gln Gly Val Leu Thr His Gly Arg Val Arg Leu Leu Ser Lys Gly  
65 70 75 80  
His Ser Cys Tyr Arg Pro Arg Arg Thr Gly Glu Arg Lys Arg Lys Ser  
85 90 95  
Val Arg Gly Cys Ile Val Asp Ala Asn Leu Ser Val Leu Asn Leu Val  
100 105 110  
Ile Val Lys Lys Gly Glu Lys Asp Ile Pro Gly Leu Thr Asp Thr Thr  
115 120 125  
Val Pro Arg Arg Leu Gly Pro Lys Arg Ala Ser Arg Ile Arg Lys Arg  
130 135 140  
Phe Asn Leu Ser Lys Glu Asp Asp Val Arg Gln Tyr Val Val Arg Lys  
145 150 155 160  
Pro Leu Asn Lys Glu Gly Lys Lys Pro Arg Thr Lys Ala Pro Lys Ile  
165 170 175  
Gln Arg Leu Val Thr Pro Arg Val Leu Gln His Lys Arg Arg Ile  
180 185 190  
Ala Leu Lys Gln Gln Arg Thr Lys Lys Asn Lys Glu Glu Ala Ala Glu  
195 200 205  
Tyr Ala Lys Leu Leu Ala Lys Arg Met Lys Glu Ala Lys Glu Lys Arg  
210 215 220  
Gln Glu Gln Ile Ala Lys Arg Arg Arg Leu Ser Ser Leu Arg Ala Ser  
225 230 235 240  
Thr Ser Lys Ser Glu Ser Ser Gln Lys  
245  
<210> 164  
<211> 469  
<212> PRT  
<213> Homo sapiens  
<400> 164  
Met His Ser Phe Pro Pro Leu Leu Leu Leu Phe Trp Gly Val Val  
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Ser His Ser Phe Pro Ala Thr Leu Glu Thr Gln Glu Asp Val Asp  
20 25 30  
Leu Val Gln Lys Tyr Leu Glu Lys Tyr Tyr Asn Leu Lys Asn Asp Gly  
35 40 45  
Arg Gln Val Glu Lys Arg Arg Asn Ser Gly Pro Val Val Glu Lys Leu  
50 55 60  
Lys Gln Met Gln Glu Phe Gly Leu Lys Val Thr Gly Lys Pro Asp  
65 70 80

Ala Glu Thr Leu Lys Val Met Lys Gln Pro Arg Cys Gly Val Pro Asp 95  
85  
Val Ala Gln Phe Val Leu Thr Glu Gly Asn Pro Arg Trp Glu Gln Thr 110  
100  
His Leu Thr Tyr Arg Ile Glu Asn Tyr Thr Pro Asp Leu Pro Arg Ala 125  
115  
Asp Val Asp His Ala Ile Glu Lys Ala Phe Gln Leu Trp Ser Asn Val 140  
130  
Thr Pro Leu Thr Phe Thr Lys Val Ser Glu Gly Gln Ala Asp Ile Met 160  
145  
Ile Ser Phe Val Arg Gly Asp His Arg Asp Asn Ser Pro Phe Asp Gly 175  
165  
Pro Gly Gly Asn Leu Ala His Ala Phe Gln Pro Gly Pro Gly Ile Gly 190  
180  
Gly Asp Ala His Phe Asp Glu Asp Glu Arg Trp Thr Asn Asn Phe Arg 205  
195  
Glu Tyr Asn Leu His Arg Val Ala Ala His Glu Leu Gly His Ser Leu 220  
210  
Gly Leu Ser His Ser Thr Asp Ile Gly Ala Leu Met Tyr Pro Ser Tyr 240  
225  
Thr Phe Ser Gly Asp Val Gln Leu Ala Gln Asp Asp Ile Asp Gly Ile 255  
245  
Gln Ala Ile Tyr Gly Arg Ser Gln Asn Pro Val Gln Pro Ile Gly Pro 270  
260  
Gln Thr Pro Lys Ala Cys Asp Ser Lys Leu Thr Phe Asp Ala Ile Thr 285  
275  
Thr Ile Arg Gly Glu Val Met Phe Phe Lys Asp Arg Phe Tyr Met Arg 300  
290  
Thr Asn Pro Phe Tyr Pro Glu Val Glu Leu Asn Phe Ile Ser Val Phe 320  
305  
Trp Pro Gln Leu Pro Asn Gly Leu Glu Ala Tyr Glu Phe Ala Asp 335  
325  
Arg Asp Glu Val Arg Phe Phe Lys Gly Asn Lys Tyr Trp Ala Val Gln 350  
340  
Gly Gln Asn Val Leu His Gly Tyr Pro Lys Asp Ile Tyr Ser Ser Phe 365  
355  
Gly Phe Pro Arg Thr Val Lys His Ile Asp Ala Ala Leu Ser Glu Glu 380  
370  
Asn Thr Gly Lys Thr Tyr Phe Phe Val Ala Asn Lys Tyr Trp Arg Tyr 400  
395

Asp Glu Tyr Lys Arg Ser Met Asp Pro Gly Tyr Pro Lys Met Ile Ala 415  
405  
His Asp Phe Pro Gly Ile Gly His Lys Val Asp Ala Val Phe Met Lys 430  
420  
Asp Gly Phe Phe Tyr Phe Phe His Gly Thr Arg Gln Tyr Lys Phe Asp 445  
435  
Pro Lys Thr Lys Arg Ile Leu Thr Leu Gln Lys Ala Asn Ser Trp Phe 460  
450  
Asn Cys Arg Lys Asn 465  
<210> 165  
<211> 166  
<212> PRT  
<213> Homo sapiens  
<400> 165  
Met Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu Glu 15  
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Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln Asp 30  
20  
Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly Lys 45  
35  
Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys Glu 60  
50  
Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly Ala Lys Lys Arg 80  
65  
Lys Lys Lys Ser Tyr Thr Thr Pro Lys Lys Asn Lys His Lys Arg Lys 95  
85  
Lys Val Lys Leu Ala Val Leu Lys Tyr Tyr Lys Val Asp Glu Asn Gly 110  
100  
Lys Ile Ser Arg Leu Arg Arg Glu Cys Pro Ser Asp Glu Cys Gly Ala 125  
115  
Gly Val Phe Met Ala Ser His Phe Asp Arg His Tyr Cys Gly Lys Cys 140  
130  
Cys Leu Thr Tyr Cys Phe Asn Lys Pro Glu Asp Lys 155  
145  
<210> 166  
<211> 783  
<212> PRT  
<213> Homo sapiens  
<400> 166  
Met Ala Lys Tyr Asn Thr Gly Gly Asn Pro Thr Glu Asp Val Ser Val 15  
1

Asn Ser Arg Pro Phe Arg Val Thr Gly Pro Asn Ser Ser Gly Ile  
 20 25 30  
 Gln Ala Arg Lys Asn Leu Phe Asn Asn Gln Gly Asn Ala Ser Pro Pro  
 35 40 45  
 Ala Gly Pro Ser Asn Val Pro Lys Phe Gly Ser Pro Lys Pro Pro Val  
 50 55 60  
 Ala Val Lys Pro Ser Ser Glu Glu Lys Pro Asp Lys Glu Pro Lys Pro  
 65 70 75  
 Pro Phe Leu Lys Pro Thr Gly Ala Gly Gln Arg Phe Gly Thr Pro Ala  
 85 90 95  
 Ser Leu Thr Thr Arg Asp Pro Glu Ala Lys Val Gly Phe Leu Lys Pro  
 100 105 110  
 Val Gly Pro Lys Pro Ile Asn Leu Pro Lys Glu Asp Ser Lys Pro Thr  
 115 120 125  
 Phe Pro Trp Pro Pro Gly Asn Lys Pro Ser Leu His Ser Val Asn Gln  
 130 135 140  
 Asp His Asp Leu Lys Pro Leu Gly Pro Lys Ser Gly Pro Thr Pro Pro  
 145 150 155 160  
 Thr Ser Glu Asn Glu Gln Lys Gln Ala Phe Pro Lys Leu Thr Gly Val  
 165 170 175  
 Lys Gly Lys Phe Met Ser Ala Ser Gln Asp Leu Glu Pro Lys Pro Leu  
 180 185 190  
 Phe Pro Lys Pro Ala Phe Gly Gln Lys Pro Pro Leu Ser Thr Glu Asn  
 195 200 205  
 Ser His Glu Asp Glu Ser Pro Met Lys Asn Val Ser Ser Ser Lys Gly  
 210 215 220  
 Ser Pro Ala Pro Leu Gly Val Arg Ser Lys Ser Gly Pro Leu Lys Pro  
 225 230 235 240  
 Ala Arg Glu Asp Ser Glu Asn Lys Asp His Ala Gly Glu Ile Ser Ser  
 245 250 255  
 Leu Pro Phe Pro Gly Val Val Leu Lys Pro Ala Ala Ser Arg Gly Gly  
 260 265 270  
 Leu Gly Leu Ser Lys Asn Gly Glu Glu Lys Lys Glu Asp Arg Lys Ile  
 275 280 285  
 Asp Ala Ala Lys Asn Thr Phe Gln Ser Lys Ile Asn Gln Glu Glu Leu  
 290 295 300  
 Ala Ser Gly Thr Pro Pro Ala Arg Phe Pro Lys Ala Pro Ser Lys Leu  
 305 310 315 320  
 Thr Val Gly Gly Pro Trp Gly Gln Ser Gln Glu Lys Glu Lys Gly Asp  
 325 330 335

Lys Asn Ser Ala Thr Pro Lys Gln Lys Pro Leu Pro Pro Leu Phe Thr  
 340 345 350  
 Leu Gly Pro Pro Pro Lys Pro Asn Arg Pro Pro Asn Val Asp Leu  
 355 360 365  
 Thr Lys Phe His Lys Thr Ser Ser Gly Asn Ser Thr Ser Lys Gly Gln  
 370 375 380  
 Thr Ser Tyr Ser Thr Thr Ser Leu Pro Pro Pro Pro Ser His Pro  
 385 390 395 400  
 Ala Ser Gln Pro Pro Leu Pro Ala Ser His Pro Ser Gln Pro Pro Val  
 405 410 415  
 Pro Ser Leu Pro Pro Arg Asn Ile Lys Pro Pro Phe Asp Leu Lys Ser  
 420 425 430  
 Pro Val Asn Glu Asp Asn Gln Asp Gly Val Thr His Ser Asp Gly Ala  
 435 440 445  
 Gly Asn Leu Asp Glu Glu Gln Asp Ser Glu Gly Glu Thr Tyr Glu Asp  
 450 455 460  
 Ile Glu Ala Ser Lys Glu Arg Glu Lys Lys Arg Glu Lys Glu Glu Lys  
 465 470 475 480  
 Lys Arg Leu Glu Leu Glu Lys Lys Glu Gln Lys Glu Lys Glu Lys Lys  
 485 490 495  
 Glu Gln Glu Ile Lys Lys Lys Phe Lys Leu Thr Gly Pro Ile Gln Val  
 500 505 510  
 Ile His Leu Ala Lys Ala Cys Asp Val Lys Gly Gly Lys Asn Glu  
 515 520 525  
 Leu Ser Phe Lys Gln Gly Glu Gln Ile Glu Ile Ile Arg Ile Thr Asp  
 530 535 540  
 Asn Pro Glu Gly Lys Trp Leu Gly Arg Thr Ala Arg Gly Ser Tyr Gly  
 545 550 555 560  
 Tyr Ile Lys Thr Thr Ala Val Glu Ile Asp Tyr Asp Ser Leu Lys Leu  
 565 570 575  
 Lys Lys Asp Ser Leu Gly Ala Pro Ser Arg Pro Ile Glu Asp Asp Gln  
 580 585 590  
 Glu Val Tyr Asp Asp Val Ala Glu Gln Asp Asp Ile Ser Ser His Ser  
 595 600 605  
 Gln Ser Gly Ser Gly Ile Phe Pro Pro Pro Pro Asp Asp Ile  
 610 615 620  
 Tyr Asp Gly Ile Glu Glu Glu Asp Ala Asp Asp Gly Phe Pro Ala Pro  
 625 630 635 640  
 Pro Lys Gln Leu Asp Met Gly Asp Glu Val Tyr Asp Asp Val Asp Thr  
 645 650 655



Ser Asp Phe Pro Val Ser Ser Ala Glu Met Ser Gln Gly Thr Asn Phe  
860 870

Gly Lys Ala Lys Thr Glu Glu Lys Asp Leu Lys Lys Leu Lys Lys Lys  
675 685

Glu Lys Glu Glu Lys Asp Phe Arg Lys Lys Phe Lys Tyr Asp Gly Glu  
690 700

Ile Arg Val Leu Tyr Ser Thr Lys Val Thr Thr Ser Ile Thr Ser Lys  
705 710 715 720

Lys Trp Gly Thr Arg Asp Leu Gln Val Lys Pro Gly Glu Ser Leu Glu  
725 730 735

Val Ile Gln Thr Thr Asp Asp Thr Lys Val Leu Cys Arg Asn Glu Glu  
740 745 750

Gly Lys Tyr Gly Tyr Val Leu Arg Ser Tyr Leu Ala Asp Asn Asp Gly  
755 760 765

Glu Ile Tyr Asp Asp Ile Ala Asp Gly Cys Ile Tyr Asp Asn Asp  
770 775 780

<210> 167  
<211> 117  
<212> PRT  
<213> Homo sapiens  
<400> 167

Met Ala Ala Ala Ala Ala Gly Ser Gly Thr Pro Arg Glu Glu Glu  
1 5 10 15

Val Pro Ala Gly Glu Ala Ala Ala Ser Gln Pro Gln Ala Pro Thr Ser  
20 25 30

Val Pro Gly Ala Arg Leu Ser Arg Leu Pro Leu Ala Arg Val Lys Ala  
35 40 45

Leu Val Lys Ala Asp Pro Asp Val Thr Leu Ala Gly Gln Glu Ala Ile  
50 55 60

Phe Ile Leu Ala Arg Ala Ala Glu Leu Phe Val Glu Thr Ile Ala Lys  
65 70 75 80

Asp Ala Tyr Cys Cys Ala Gln Gln Gly Lys Arg Lys Thr Leu Gln Arg  
85 90 95

Arg Asp Leu Asp Asn Ala Ile Glu Ala Val Asp Glu Phe Ala Phe Leu.  
100 105 110

Glu Gly Thr Leu Asp  
115

<210> 168  
<211> 243  
<212> PRT  
<213> Homo sapiens  
<400> 168

Met Ala Val Gln Ile Ser Lys Arg Arg Lys Phe Val Ala Asp Gly Ile  
1 5 10 15

Phe Lys Ala Glu Leu Asn Glu Phe Leu Thr Arg Glu Leu Ala Glu Asp  
20 25 30

Gly Tyr Ser Gly Val Glu Val Arg Val Thr Pro Thr Arg Thr Glu Ile  
35 40 45

Ile Ile Leu Ala Thr Arg Thr Gln Asn Val Leu Gly Glu Lys Gly Arg  
50 55 60

Arg Ile Arg Glu Leu Thr Ala Val Val Gln Lys Arg Phe Gly Phe Pro  
65 70 75 80

Glu Gly Ser Val Glu Leu Tyr Ala Glu Lys Val Ala Thr Arg Gly Leu  
85 90 95

Cys Ala Ile Ala Gln Ala Glu Ser Leu Arg Tyr Lys Leu Leu Gly Gly  
100 105 110

Leu Ala Val Arg Arg Ala Cys Tyr Gly Val Leu Arg Phe Ile Met Glu  
115 120 125

Ser Gly Ala Lys Gly Cys Glu Val Val Ser Gly Lys Leu Arg Gly  
130 135 140

Gln Arg Ala Lys Ser Met Lys Phe Val Asp Gly Leu Met Ile His Ser  
145 150 155 160

Gly Asp Pro Val Asn Tyr Tyr Val Asp Thr Ala Val Arg His Val Leu  
165 170 175

Leu Arg Gln Gly Val Leu Gly Ile Lys Val Lys Ile Met Leu Pro Trp  
180 185 190

Asp Pro Thr Gly Lys Ile Gly Pro Lys Lys Pro Leu Pro Asp His Val  
195 200 205

Ser Ile Val Glu Pro Lys Asp Glu Ile Leu Pro Thr Thr Pro Ile Ser  
210 215 220

Glu Gln Lys Gly Gly Lys Pro Glu Pro Ala Met Pro Gln Pro Val  
225 230 235 240

Pro Thr Ala

<210> 169  
<211> 136  
<212> PRT  
<213> Homo sapiens  
<400> 169

Met Val Leu Leu Glu Ser Glu Gln Phe Leu Thr Glu Leu Thr Arg Leu  
1 5 10 15

Phe Gln Lys Cys Arg Thr Ser Gly Ser Val Tyr Ile Thr Leu Lys Lys  
20 25 30



Gly Leu Ser Gly Ala Gly Lys Thr Thr Ile Ser Phe Ala Leu Glu Glu  
50 60

Tyr Leu Val Ser His Ala Ile Pro Cys Tyr Ser Leu Asp Gly Asp Asn  
65 75

Val Arg His Gly Leu Asn Arg Asn Leu Gly Phe Ser Pro Gly Asp Arg  
85 95

Glu Glu Asn Ile Arg Arg Ile Ala Glu Val Ala Lys Leu Phe Ala Asp  
100 110

Ala Gly Leu Val Cys Ile Thr Ser Phe Ile Ser Pro Phe Ala Lys Asp  
115 125

Arg Glu Asn Ala Arg Lys Ile His Glu Ser Ala Gly Leu Pro Phe Phe  
130 140

Glu Ile Phe Val Asp Ala Pro Leu Asn Ile Cys Glu Ser Arg Asp Val  
145 160

Lys Gly Leu Tyr Lys Lys Ala Arg Ala Gly Glu Ile Lys Gly Phe Thr  
165 175

Gly Ile Asp Ser Asp Tyr Glu Lys Pro Glu Thr Pro Glu Arg Val Leu  
180 190

Lys Thr Asn Leu Ser Thr Val Ser Asp Cys Val His Glu Val Val Glu  
195 205

Leu Leu Glu Glu Cln Asn Ile Val Pro Tyr Thr Ile Ile Lys Asp Ile  
210 220

His Glu Leu Phe Val Pro Glu Asn Lys Leu Asn His Val Arg Ala Glu  
225 235

Ala Glu Thr Leu Pro Ser Leu Ser Ile Thr Lys Leu Asp Leu Glu Thr  
245 255

Val Glu Val Leu Ser Glu Gly Trp Ala Thr Pro Leu Lys Gly Phe Met  
260 270

Arg Glu Lys Glu Tyr Leu Glu Val Met His Phe Asp Thr Leu Leu Asp  
275 285

Asp Gly Val Ile Asn Met Ser Ile Pro Ile Val Leu Pro Val Ser Ala  
290 300

Glu Asp Lys Thr Arg Leu Glu Gly Cys Ser Lys Phe Val Leu Ala His  
305 315

Gly Gly Arg Arg Val Ala Ile Leu Arg Asp Ala Glu Phe Tyr Glu His  
325 335

Arg Lys Glu Glu Arg Cys Ser Arg Val Trp Gly Thr Thr Cys Thr Lys  
340 350

His Pro His Ile Lys Lys Met Val Met Glu Ser Gly Asp Trp Leu Val Gly  
355 365

Gly Asp Leu Glu Val Leu Glu Lys Ile Arg Trp Asn Asp Gly Leu Asp  
370 380

Gln Tyr Arg Leu Thr Pro Leu Glu Leu Lys Glu Lys Cys Lys Glu Met  
385 395

Asn Ala Asp Ala Val Phe Ala Phe Glu Leu Arg Asn Pro Val His Asn  
405 415

Gly His Ala Leu Leu Met Gln Asp Thr Arg Arg Arg Leu Leu Glu Arg  
420 430

Gly Tyr Lys His Pro Val Leu Leu Leu His Pro Leu Gly Gly Trp Thr  
435 445

Lys Asp Asp Asp Val Pro Leu Asp Trp Arg Met Lys Glu His Ala Ala  
450 460

Val Leu Glu Glu Gly Val Leu Asp Pro Lys Ser Thr Ile Val Ala Ile  
465 475

Phe Pro Ser Pro Met Leu Tyr Ala Gly Pro Thr Glu Val Gln Trp His  
485 495

Cys Arg Ser Arg Met Ile Ala Gly Ala Asn Phe Tyr Ile Val Gly Arg  
500 510

Asp Pro Ala Gly Met Pro His Pro Glu Thr Lys Lys Asp Leu Tyr Glu  
515 525

Pro Thr His Gly Gly Lys Val Leu Ser Met Ala Pro Gly Leu Thr Ser  
530 540

Val Glu Ile Ile Pro Phe Arg Val Ala Ala Tyr Asn Lys Ala Lys Lys  
545 555

Ala Met Asp Phe Tyr Asp Leu Ala Arg His Asn Glu Phe Asp Phe Ile  
560 575

Ser Gly Thr Arg Met Arg Lys Leu Ala Arg Glu Gly Glu Asn Pro Pro  
580 590

Asp Gly Phe Met Ala Pro Lys Ala Trp Lys Val Leu Thr Asp Tyr Tyr  
595 605

Arg Ser Leu Glu Lys Asn  
610

<210> 172  
<211> 798  
<212> PRT  
<213> Homo sapiens  
  
<400> 172

Met Asn Leu Glu Pro Ile Phe Trp Ile Gly Leu Ile Ser Ser Val Cys  
1 15

Cys Val Phe Ala Glu Thr Asp Glu Asn Arg Cys Leu Lys Ala Asn Ala  
20 25 30

Lys Ser Cys Gly Glu Cys Ile Gln Ala Gly Pro Asn Cys Gly Trp Cys  
 35 40 45  
 Thr Asn Ser Thr Phe Leu Gln Glu Gly Met Pro Thr Ser Ala Arg Cys  
 50 55 60  
 Asp Asp Leu Glu Ala Leu Lys Lys Cys Gly Cys Pro Pro Asp Asp Ile  
 65 70 75 80  
 Glu Asn Pro Arg Gly Ser Lys Asp Ile Lys Lys Asn Lys Asn Val Thr  
 85 90 95  
 Asn Arg Ser Lys Gly Thr Ala Glu Lys Leu Lys Pro Glu Asp Ile His  
 100 105 110  
 Gln Ile Gln Pro Gln Gln Leu Val Leu Arg Leu Arg Ser Gly Glu Pro  
 115 120 125  
 Gln Thr Phe Thr Leu Lys Phe Lys Arg Ala Glu Asp Tyr Pro Ile Asp  
 130 135 140  
 Leu Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp Asp Leu Glu  
 145 150 155 160  
 Asn Val Lys Ser Leu Gly Thr Asp Leu Met Asn Glu Met Arg Arg Ile  
 165 170 175  
 Thr Ser Asp Phe Arg Ile Gly Phe Gly Ser Phe Val Glu Lys Thr Val  
 180 185 190  
 Met Pro Tyr Ile Ser Thr Thr Pro Ala Lys Leu Arg Asn Pro Cys Thr  
 195 200 205  
 Ser Glu Gln Asn Cys Thr Thr Pro Phe Ser Tyr Lys Asn Val Leu Ser  
 210 215 220  
 Leu Thr Asn Lys Gly Glu Val Phe Asn Glu Leu Val Gly Lys Gln Arg  
 225 230 235 240  
 Ile Ser Gly Asn Leu Asp Ser Pro Glu Gly Gly Phe Asp Ala Ile Met  
 245 250 255  
 Gln Val Ala Val Cys Gly Ser Leu Ile Gly Trp Arg Asn Val Thr Arg  
 260 265 270  
 Leu Leu Val Phe Ser Thr Asp Ala Gly Phe His Phe Ala Gly Asp Gly  
 275 280 285  
 Lys Leu Gly Gly Ile Val Leu Pro Asn Asp Gly Gln Cys His Leu Glu  
 290 295 300  
 Asn Asn Met Tyr Thr Met Ser His Tyr Tyr Asp Tyr Pro Ser Ile Ala  
 305 310 315 320  
 His Leu Val Gln Lys Leu Ser Glu Asn Asn Ile Gln Thr Ile Phe Ala  
 325 330 335  
 Val Thr Glu Glu Phe Gln Pro Val Tyr Lys Glu Leu Lys Asn Leu Ile

340 345 350  
 Pro Lys Ser Ala Val Gly Thr Leu Ser Ala Asn Ser Ser Asn Val Ile  
 355 360 365  
 Gln Leu Ile Ile Asp Ala Tyr Asn Ser Leu Ser Ser Glu Val Ile Leu  
 370 375 380  
 Glu Asn Gly Lys Leu Ser Glu Gly Val Thr Ile Ser Tyr Lys Ser Tyr  
 385 390 395 400  
 Cys Lys Asn Gly Val Asn Gly Thr Gly Glu Asn Gly Arg Lys Cys Ser  
 405 410 415  
 Asn Ile Ser Ile Gly Asp Glu Val Gln Phe Glu Ile Ser Ile Thr Ser  
 420 425 430  
 Asn Lys Cys Pro Lys Lys Asp Ser Asp Ser Phe Lys Ile Arg Pro Leu  
 435 440 445  
 Gly Phe Thr Glu Glu Val Glu Val Ile Leu Gln Tyr Ile Cys Glu Cys  
 450 455 460  
 Glu Cys Gln Ser Glu Gly Ile Pro Glu Ser Pro Lys Cys His Glu Gly  
 465 470 475 480  
 Asn Gly Thr Phe Glu Cys Gly Ala Cys Arg Cys Asn Glu Gly Arg Val  
 485 490 495  
 Gly Arg His Cys Glu Cys Ser Thr Asp Glu Val Asn Ser Glu Asp Met  
 500 505 510  
 Asp Ala Tyr Cys Arg Lys Glu Asn Ser Ser Glu Ile Cys Ser Asn Asn  
 515 520 525  
 Gly Glu Cys Val Cys Gly Gln Cys Val Cys Arg Lys Arg Asp Asn Thr  
 530 535 540  
 Asn Glu Ile Tyr Ser Gly Lys Phe Cys Glu Cys Asp Asn Phe Asn Cys  
 545 550 555 560  
 Asp Arg Ser Asn Gly Leu Ile Cys Gly Gly Asn Gly Val Cys Lys Cys  
 565 570 575  
 Arg Val Cys Glu Cys Asn Pro Asn Tyr Thr Gly Ser Ala Cys Asp Cys  
 580 585 590  
 Ser Leu Asp Thr Ser Thr Cys Glu Ala Ser Asn Gly Gln Ile Cys Asn  
 595 600 605  
 Gly Arg Gly Ile Cys Glu Cys Gly Val Cys Lys Cys Thr Asp Pro Lys  
 610 615 620  
 Phe Gln Gly Gln Thr Cys Glu Met Cys Gln Thr Cys Leu Gly Val Cys  
 625 630 635 640  
 Ala Glu His Lys Glu Cys Val Gln Cys Arg Ala Phe Asn Lys Gly Glu  
 645 650 655

Lys Lys Asp Thr Cys Thr Gln Glu Cys Ser Tyr Phe Asn Ile Thr Lys  
 860 865 870  
 Val Glu Ser Arg Asp Lys Leu Pro Gln Pro Val Gln Pro Asp Pro Val  
 875 880 885  
 Ser His Cys Lys Glu Lys Asp Val Asp Asp Cys Trp Phe Tyr Phe Thr  
 890 895 900  
 Tyr Ser Val Asn Gly Asn Asn Glu Val Met Val His Val Val Glu Asn  
 905 910 915 920  
 Pro Glu Cys Pro Thr Gly Pro Asp Ile Ile Pro Ile Val Ala Gly Val  
 925 930 935  
 Val Ala Gly Ile Val Leu Ile Gly Leu Ala Leu Leu Ile Trp Lys  
 940 945 950  
 Leu Leu Met Ile Ile His Asp Arg Arg Glu Phe Ala Lys Phe Glu Lys  
 955 960 965  
 Glu Lys Met Asn Ala Lys Trp Asp Thr Gly Glu Asn Pro Ile Tyr Lys  
 970 975 980  
 Ser Ala Val Thr Thr Val Val Asn Pro Lys Tyr Glu Gly Lys  
 985 990 995  
 <210> 173  
 <211> 302  
 <212> PRT  
 <213> Homo sapiens  
 <400> 173  
 Met Ser Lys Lys Leu Gly Ala Asp Phe His Gly Thr Phe Ser Tyr  
 1 5 10 15  
 Leu Asp Asp Val Pro Phe Lys Thr Gly Asp Lys Phe Lys Thr Pro Ala  
 20 25 30  
 Lys Val Gly Leu Pro Ile Gly Phe Ser Leu Pro Asp Cys Leu Gln Val  
 35 40 45  
 Val Arg Glu Val Gln Tyr Asp Phe Ser Leu Glu Lys Lys Thr Ile Glu  
 50 55 60  
 Trp Ala Glu Glu Ile Lys Lys Ile Glu Glu Ala Glu Arg Glu Ala Glu  
 65 70 75 80  
 Cys Lys Ile Ala Glu Ala Glu Ala Lys Val Asn Ser Lys Ser Gly Pro  
 85 90 95  
 Glu Gly Asp Ser Lys Met Ser Phe Ser Lys Thr His Ser Thr Ala Thr  
 100 105 110  
 Met Pro Pro Ile Asn Pro Ile Leu Ala Ser Leu Gln His Asn Ser  
 115 120 125  
 Ile Leu Thr Pro Thr Arg Val Ser Ser Ala Thr Lys Lys Gln Lys Val  
 130 135 140

Leu Ser Pro Pro His Ile Lys Ala Asp Phe Asn Leu Ala Asp Phe Glu  
 145 150 155 160  
 Cys Glu Glu Asp Pro Phe Asp Asn Leu Glu Leu Lys Thr Ile Asp Glu  
 165 170 175  
 Lys Glu Glu Leu Arg Asn Ile Leu Val Gly Thr Thr Gly Pro Ile Met  
 180 185 190  
 Ala Gln Leu Leu Asp Asn Asn Leu Pro Arg Gly Gly Ser Gly Ser Val  
 195 200 205  
 Leu Gln Asp Glu Glu Val Leu Ala Ser Leu Glu Arg Ala Thr Leu Asp  
 210 215 220  
 Phe Lys Pro Leu His Lys Pro Asn Gly Phe Ile Thr Leu Pro Gln Leu  
 225 230 235 240  
 Gly Asn Cys Glu Lys Met Ser Leu Ser Ser Lys Val Ser Leu Pro Pro  
 245 250 255  
 Ile Pro Ala Val Ser Asn Ile Lys Ser Leu Ser Phe Pro Lys Leu Asp  
 260 265 270  
 Ser Asp Asp Ser Asn Gln Lys Thr Ala Lys Leu Ala Ser Thr Phe His  
 275 280 285  
 Ser Thr Ser Cys Leu Arg Asn Gly Thr Phe Gln Asn Ser Leu Lys Pro  
 290 295 300  
 Ser Thr Gln Ser Ser Ala Ser Glu Leu Asn Gly His His Thr Leu Gly  
 305 310 315 320  
 Leu Ser Ala Leu Asn Leu Asp Ser Gly Thr Glu Met Pro Ala Leu Thr  
 325 330 335  
 Ser Ser Gln Met Pro Ser Leu Ser Val Leu Ser Val Cys Thr Glu Glu  
 340 345 350  
 Ser Ser Pro Pro Asn Thr Gly Pro Thr Val Thr Pro Pro Asn Phe Ser  
 355 360 365  
 Val Ser Gln Val Pro Asn Met Pro Ser Cys Pro Gln Ala Tyr Ser Glu  
 370 375 380  
 Leu Gln Met Leu Ser Pro Ser Glu Arg Gln Cys Val Glu Thr Val Val  
 385 390 395 400  
 Asn Met Gly Tyr Ser Tyr Glu Cys Val Leu Arg Ala Met Lys Lys  
 405 410 415  
 Gly Glu Asn Ile Glu Gln Ile Leu Asp Tyr Leu Phe Ala His Gly Gln  
 420 425 430  
 Leu Cys Glu Lys Gly Phe Asp Pro Leu Leu Val Glu Glu Ala Leu Glu  
 435 440 445  
 Met His Gln Cys Ser Glu Glu Lys Met Met Glu Phe Leu Gln Leu Met  
 450 455 460

Ser Lys Phe Lys Glu Met Gly Phe Glu Leu Lys Asp Ile Lys Glu Val  
465 470 475 480  
Leu Leu His Asn Asn Asp Gln Asp Asn Ala Leu Glu Asp Leu Met  
485 490 495  
Ala Arg Ala Gly Ala Ser  
500  
<210> 174  
<211> 545  
<212> PRT  
<213> Homo sapiens  
<400> 174  
Met Ser Asn Asn Gly Leu Asp Ile Gln Asp Lys Pro Pro Ala Pro Pro  
1 10 15  
Met Arg Asn Thr Ser Thr Met Ile Gly Val Gly Ser Lys Asp Ala Gly  
20 25 30  
Thr Leu Asn His Gly Ser Lys Pro Leu Pro Pro Asn Pro Glu Glu Lys  
35 40 45  
Lys Lys Lys Asp Arg Phe Tyr Arg Ser Ile Leu Pro Gly Asp Lys Thr  
50 55 60  
Asn Lys Lys Lys Glu Lys Glu Arg Pro Glu Ile Ser Leu Pro Ser Asp  
65 70 75 80  
Phe Glu His Thr Ile His Val Gly Phe Asp Ala Val Thr Gly Glu Phe  
85 90 95  
Thr Gly Met Pro Glu Gln Thr Ala Arg Leu Leu Gln Thr Ser Asn Ile  
100 105 110  
Thr Lys Ser Glu Gln Lys Lys Asn Pro Gln Ala Val Leu Asp Val Leu  
115 120 125  
Glu Phe Tyr Asn Ser Lys Lys Thr Ser Asn Ser Gln Lys Tyr Met Ser  
130 135 140  
Phe Thr Asp Lys Ser Ala Glu Asp Tyr Asn Ser Ser Asn Ala Leu Asn  
145 150 155 160  
Val Lys Ala Val Ser Glu Thr Pro Ala Val Pro Pro Val Ser Glu Asp  
165 170 175  
Glu Asp Asp Asp Asp Asp Ala Thr Pro Pro Pro Val Ile Ala Pro  
180 185 190  
Arg Pro Glu His Thr Lys Ser Val Tyr Thr Arg Ser Val Ile Glu Pro  
195 200 205  
Leu Pro Val Thr Pro Thr Arg Asp Val Ala Thr Ser Pro Ile Ser Pro  
210 215 220  
Thr Glu Asn Asn Thr Thr Pro Pro Asp Ala Leu Thr Arg Asn Thr Glu  
225 230 235

Lys Gln Lys Lys Lys Pro Lys Met Ser Asp Glu Glu Ile Leu Glu Lys  
245 250 255  
Leu Arg Ser Ile Val Ser Val Gly Asp Pro Lys Lys Tyr Thr Arg  
260 265 270  
Phe Glu Lys Ile Gly Gln Gly Ala Ser Gly Thr Val Tyr Thr Ala Met  
275 280 285  
Asp Val Ala Thr Gly Gln Glu Val Ala Ile Lys Gln Met Asn Leu Gln  
290 295 300  
Gln Gln Pro Lys Lys Glu Leu Ile Ile Asn Glu Ile Leu Val Met Arg  
305 310 315 320  
Glu Asn Lys Asn Pro Asn Ile Val Asn Tyr Leu Asp Ser Tyr Leu Val  
325 330 335  
Gly Asp Glu Leu Trp Val Val Met Glu Tyr Leu Ala Gly Gly Ser Leu  
340 345 350  
Thr Asp Val Val Thr Glu Thr Cys Met Asp Glu Gly Gln Ile Ala Ala  
355 360 365  
Val Cys Arg Glu Cys Leu Gln Ala Leu Glu Phe Leu His Ser Asn Gln  
370 375 380  
Val Ile His Arg Asp Ile Lys Ser Asp Asn Ile Leu Leu Gly Met Asp  
385 390 395 400  
Gly Ser Val Lys Leu Thr Asp Phe Gly Phe Cys Ala Gln Ile Thr Pro  
405 410 415  
Glu Gln Ser Lys Arg Ser Thr Met Val Gly Thr Pro Tyr Trp Met Ala  
420 425 430  
Pro Glu Val Val Thr Arg Lys Ala Tyr Gly Pro Lys Val Asp Ile Trp  
435 440 445  
Ser Leu Gly Ile Met Ala Ile Glu Met Ile Glu Gly Glu Pro Pro Tyr  
450 455 460  
Leu Asn Glu Asn Pro Leu Arg Ala Leu Tyr Leu Ile Ala Thr Asn Gly  
465 470 475 480  
Thr Pro Glu Leu Gln Asn Pro Glu Lys Leu Ser Ala Ile Phe Arg Asp  
485 490 495  
Phe Leu Asn Arg Cys Leu Asp Met Asp Val Glu Lys Arg Gly Ser Ala  
500 505 510  
Lys Glu Leu Leu Gln His Gln Phe Leu Lys Ile Ala Lys Pro Leu Ser  
515 520 525  
Ser Leu Thr Pro Leu Ile Ala Ala Ala Lys Glu Ala Thr Lys Asn Asn  
530 535 540  
His  
545

<210> 175  
<211> 1360  
<212> PRT  
<213> Homo sapiens  
  
<400> 175  
Met Ser Arg Gln Ser Thr Leu Tyr Ser Phe Pro Lys Ser Pro Ala 15  
1 10  
Leu Ser Asp Ala Asn Lys Ala Ser Ala Arg Ala Ser Arg Glu Gly Gly 30  
20 25  
Arg Ala Ala Ala Pro Gly Ala Ser Pro Ser Pro Gly Gly Asp Ala 45  
35 40  
Ala Trp Ser Glu Ala Gly Pro Gly Pro Arg Pro Leu Ala Arg Ser Ala 60  
50 55  
Ser Pro Pro Lys Ala Lys Asn Leu Asn Gly Gly Leu Arg Arg Ser Val 75  
65 70  
Ala Pro Ala Ala Pro Thr Ser Cys Asp Phe Ser Pro Gly Asp Leu Val 95  
85 90  
Trp Ala Lys Met Glu Gly Tyr Pro Trp Trp Pro Cys Leu Val Tyr Asn 110  
100 105  
His Pro Phe Asp Gly Thr Phe Ile Arg Glu Lys Gly Lys Ser Val Arg 125  
115 120  
Val His Val Gln Phe Asp Asp Ser Pro Thr Arg Gly Trp Val Ser 140  
130 135  
Lys Arg Leu Lys Pro Tyr Thr Gly Ser Lys Ser Lys Glu Ala Gln 160  
145 150  
Lys Gly Gly His Phe Tyr Ser Ala Lys Pro Glu Ile Leu Arg Ala Met 175  
165 170  
Gln Arg Ala Asp Glu Ala Leu Asn Lys Asp Lys Ile Lys Arg Leu Glu 190  
180 185  
Leu Ala Val Cys Asp Glu Pro Ser Glu Pro Glu Glu Glu Glu Met 205  
195 200  
Glu Val Gly Thr Thr Tyr Val Thr Asp Lys Ser Glu Glu Asp Asn Glu 220  
210 215  
Ile Glu Ser Glu Glu Val Gln Pro Lys Thr Gln Gly Ser Arg Arg 240  
225 230  
Ser Ser Arg Gln Ile Lys Lys Arg Arg Val Ile Ser Asp Ser Glu Ser 255  
245 250  
Asp Ile Gly Gly Ser Asp Val Glu Phe Lys Pro Asp Thr Lys Glu Glu 270  
260 265  
Gly Ser Ser Asp Glu Ile Ser Ser Gly Val Gly Asp Ser Glu Ser Glu 285  
275 280

Gly Leu Asn Ser Pro Val Lys Val Ala Arg Lys Arg Lys Arg Met Val 300  
290 295  
Thr Gly Asn Gly Ser Leu Lys Arg Lys Ser Ser Arg Lys Glu Thr Pro 320  
305 310  
Ser Ala Thr Lys Gln Ala Thr Ser Ile Ser Ser Glu Thr Lys Asn Thr 335  
325 330  
Leu Arg Ala Phe Ser Ala Pro Gln Asn Ser Glu Ser Gln Ala His Val 350  
340 345  
Ser Gly Gly Gly Asp Asp Ser Ser Arg Pro Thr Val Trp Tyr His Glu 365  
355 360  
Thr Leu Glu Trp Leu Lys Glu Glu Lys Arg Arg Asp Glu His Arg Arg 380  
370 375  
Arg Pro Asp His Pro Asp Phe Asp Ala Ser Thr Leu Tyr Val Pro Glu 400  
385 390  
Asp Phe Leu Asn Ser Cys Thr Pro Gly Met Arg Lys Trp Trp Gln Ile 415  
405 410  
Lys Ser Gln Asn Phe Asp Leu Val Ile Cys Tyr Lys Val Gly Lys Phe 430  
420 425  
Tyr Glu Leu Tyr His Met Asp Ala Leu Ile Gly Val Ser Glu Leu Gly 445  
435 440  
Leu Val Phe Met Lys Gly Asn Trp Ala His Ser Gly Phe Pro Glu Ile 460  
450 455  
Ala Phe Gly Arg Tyr Ser Asp Ser Leu Val Gln Lys Gly Tyr Lys Val 480  
465 470  
Ala Arg Val Glu Gln Thr Glu Thr Pro Glu Met Met Glu Ala Arg Cys 495  
485 490  
Arg Lys Met Ala His Ile Ser Lys Tyr Asp Arg Val Val Arg Arg Glu 510  
500 505  
Ile Cys Arg Ile Ile Thr Lys Gly Thr Gln Thr Tyr Ser Val Leu Glu 525  
515 520  
Gly Asp Pro Ser Glu Asn Tyr Ser Lys Tyr Leu Leu Ser Leu Lys Glu 540  
530 535  
Lys Glu Glu Asp Ser Ser Gly His Thr Arg Ala Tyr Gly Val Cys Phe 560  
545 550  
Val Asp Thr Ser Leu Gly Lys Phe Phe Ile Gly Gln Phe Ser Asp Asp 575  
565 570  
Arg His Cys Ser Arg Phe Arg Thr Leu Val Ala His Tyr Pro Pro Val 590  
580 585  
Gln Val Leu Phe Glu Lys Gly Asn Leu Ser Lys Glu Thr Lys Thr Ile

595	600	605	
Leu Lys Ser Ser Leu Ser Cys Ser Leu Gln Glu Gly Leu Ile Pro Gly 810			
Ser Gln Phe Trp Asp Ala Ser Lys Thr Leu Arg Thr Leu Leu Glu 625	630	635	640
Glu Tyr Phe Arg Glu Lys Leu Ser Asp Gly Ile Gly Val Met Leu Pro 643	648	653	658
Gln Val Leu Lys Gly Met Thr Ser Glu Ser Asp Ser Ile Gly Leu Thr 660	665	670	
Pro Gly Glu Lys Ser Glu Leu Ala Leu Ser Ala Leu Gly Gly Cys Val 675	680	685	
Phe Tyr Leu Lys Lys Cys Leu Ile Asp Gln Glu Leu Leu Ser Met Ala 690	695	700	
Asn Phe Glu Glu Tyr Ile Pro Leu Asp Ser Asp Thr Val Ser Thr Thr 705	710	715	720
Arg Ser Gly Ala Ile Phe Thr Lys Ala Tyr Gln Arg Met Val Leu Asp 725	730	735	
Ala Val Thr Leu Asn Asn Leu Glu Ile Phe Leu Asn Gly Thr Asn Gly 740	745	750	
Ser Thr Glu Gly Thr Leu Leu Glu Arg Val Asp Thr Cys His Thr Pro 755	760	765	
Phe Gly Lys Arg Leu Leu Lys Gln Trp Leu Cys Ala Pro Leu Cys Asn 770	775	780	
His Tyr Ala Ile Asn Asp Arg Leu Asp Ala Ile Glu Asp Leu Met Val 785	790	795	800
Val Pro Asp Lys Ile Ser Glu Val Val Glu Leu Leu Lys Lys Leu Pro 805	810	815	
Asp Leu Glu Arg Leu Leu Ser Lys Ile His Asn Val Gly Ser Pro Leu 820	825	830	
Lys Ser Gln Asn His Pro Asp Ser Arg Ala Ile Met Tyr Glu Glu Thr 835	840	845	
Thr Tyr Ser Lys Lys Lys Ile Ile Asp Phe Leu Ser Ala Leu Glu Gly 850	855	860	
Phe Lys Val Met Cys Lys Ile Ile Gly Ile Met Glu Glu Val Ala Asp 865	870	875	880
Gly Phe Lys Ser Lys Ile Leu Lys Gln Val Ile Ser Leu Gln Thr Lys 885	890	895	
Asn Pro Glu Gly Arg Phe Pro Asp Leu Thr Val Glu Leu Asn Arg Trp 900	905	910	
Asp Thr Ala Phe Asp His Glu Lys Ala Arg Lys Thr Gly Leu Ile Thr 915	920	925	
Pro Lys Ala Gly Phe Asp Ser Asp Tyr Asp Gln Ala Leu Ala Asp Ile 930	935	940	
Arg Glu Asn Glu Gln Ser Leu Leu Glu Tyr Leu Glu Lys Gln Arg Asn 945	950	955	960
Arg Ile Gly Cys Arg Thr Ile Val Tyr Trp Gly Ile Gly Arg Asn Arg 965	970	975	
Tyr Gln Leu Glu Ile Pro Glu Asn Phe Thr Thr Arg Asn Leu Pro Glu 980	985	990	
Glu Tyr Glu Leu Lys Ser Thr Lys Lys Gly Cys Lys Arg Tyr Trp Thr 995	1000	1005	
Lys Thr Ile Glu Lys Lys Leu Ala Asn Leu Ile Asn Ala Glu Glu 1010	1015	1020	
Arg Arg Asp Val Ser Leu Lys Asp Cys Met Arg Arg Leu Phe Tyr 1025	1030	1035	
Asn Phe Asp Lys Asn Tyr Lys Asp Trp Gln Ser Ala Val Glu Cys 1040	1045	1050	
Ile Ala Val Leu Asp Val Leu Leu Cys Leu Ala Asn Tyr Ser Arg 1055	1060	1065	
Gly Gly Asp Gly Pro Met Cys Arg Pro Val Ile Leu Leu Pro Glu 1070	1075	1080	
Asp Thr Pro Pro Phe Leu Glu Leu Lys Gly Ser Arg His Pro Cys 1085	1090	1095	
Ile Thr Lys Thr Phe Phe Gly Asp Asp Phe Ile Pro Asn Asp Ile 1100	1105	1110	
Leu Ile Gly Cys Glu Glu Glu Gln Gln Glu Asn Gly Lys Ala Tyr 1115	1120	1125	
Cys Val Leu Val Thr Gly Pro Asn Met Gly Gly Lys Ser Thr Leu 1130	1135	1140	
Met Arg Gln Ala Gly Leu Leu Ala Val Met Ala Gln Met Gly Cys 1145	1150	1155	
Tyr Val Pro Ala Glu Val Cys Arg Leu Thr Pro Ile Asp Arg Val 1160	1165	1170	
Phe Thr Arg Leu Gly Ala Ser Asp Arg Ile Met Ser Gly Glu Ser 1175	1180	1185	
Thr Phe Phe Val Glu Leu Ser Glu Thr Ala Ser Ile Leu Met His 1190	1195	1200	
Ala Thr Ala His Ser Leu Val Leu Val Asp Glu Leu Gly Arg Gly 1205	1210	1215	



Thr Ala Thr Phe Asp Gly Thr Ala Ile Ala Asn Ala Val Val Lys  
1220 1225 1230

Glu Leu Ala Glu Thr Ile Lys Cys Arg Thr Leu Phe Ser Thr His  
1235 1240 1245

Tyr His Ser Leu Val Glu Asp Tyr Ser Gln Asn Val Ala Val Arg  
1250 1255 1260

Leu Gly His Met Ala Cys Met Val Glu Asn Glu Cys Glu Asp Pro  
1265 1270 1275

Ser Gln Glu Thr Ile Thr Phe Leu Tyr Lys Phe Ile Lys Gly Ala  
1280 1285 1290

Cys Pro Lys Ser Tyr Gly Phe Asn Ala Ala Arg Leu Ala Asn Leu  
1295 1300 1305

Pro Glu Glu Val Ile Gln Lys Gly His Arg Lys Ala Arg Glu Phe  
1310 1315 1320

Glu Lys Met Asn Gln Ser Leu Arg Leu Phe Arg Glu Val Cys Leu  
1325 1330 1335

Ala Ser Glu Arg Ser Thr Val Asp Ala Glu Ala Val His Lys Leu  
1340 1345 1350

Leu Thr Leu Ile Lys Glu Leu  
1355 1360

<210> 176  
<211> 398  
<212> PRT  
<213> Homo sapiens  
<400> 176

Met Gln Ser Glu Arg Gly Ile Thr Ile Asp Ile Ser Leu Thr Lys Phe  
1 5 10 15

Glu Thr Ser Lys Tyr Tyr Val Thr Ile Ile Asp Ala Pro Gly His Arg  
20 25 30

Asp Phe Ile Gln Asn Met Ile Thr Gly Thr Ser Gln Ala Asp Cys Ala  
35 40 45

Val Leu Ile Val Ala Ala Gly Val Gly Glu Phe Glu Ala Gly Ile Ser  
50 55 60

Lys Asn Gly Gln Thr Arg Glu His Ala Leu Leu Ala Tyr Thr Leu Gly  
65 70 75 80

Val Lys Gln Leu Ile Val Gly Val Asn Lys Met Asp Ser Thr Glu Pro  
85 90 95

Pro Tyr Ser Gln Lys Arg Tyr Glu Glu Ile Val Lys Glu Val Ser Thr  
100 105 110

Tyr Ile Lys Lys Ile Gly Tyr Asn Pro Asp Thr Val Ala Phe Val Pro  
115 120 125

Ile Ser Gly Trp Asn Gly Asp Asn Met Leu Glu Pro Ser Ala Asn Met  
130 135 140

Pro Trp Phe Lys Gly Trp Lys Val Thr Arg Lys Asp Gly Asn Ala Ser  
145 150 155 160

Gly Thr Thr Leu Leu Glu Ala Leu Asp Cys Ile Leu Pro Pro Thr Arg  
165 170 175

Pro Thr Asp Lys Pro Leu Gly Leu Pro Leu Gln Asp Val Tyr Lys Ile  
180 185 190

Gly Gly Ile Gly Thr Val Pro Val Gly Arg Val Glu Thr Gly Val Leu  
195 200 205

Lys Pro Gly Met Val Val Thr Phe Gly Pro Val Asn Val Thr Thr Glu  
210 215 220

Val Lys Ser Val Glu Met His His Glu Ala Leu Gly Glu Ala Leu Pro  
225 230 235 240

Gly Asp Asn Val Gly Phe Asn Val Lys Asn Val Ser Val Lys Asp Val  
245 250 255

Arg Arg Gly Asn Val Ala Gly Asp Ser Lys Asn Asp Pro Pro Met Glu  
260 265 270

Ala Ala Gly Phe Pro Ala Gln Val Ile Ile Leu Asn His Pro Gly Gln  
275 280 285

Ile Ser Ala Gly Tyr Ala Pro Val Leu Asp Cys His Thr Ala His Ile  
290 295 300

Ala Cys Lys Phe Ala Glu Leu Lys Glu Lys Ile Asp Arg Arg Ser Gly  
305 310 315 320

Lys Lys Leu Glu Asp Gly Pro Lys Phe Leu Lys Ser Gly Asp Ala Ala  
325 330 335

Ile Val Asp Met Val Pro Gly Lys Pro Met Cys Val Glu Ser Phe Ser  
340 345 350

Asp Tyr Pro Pro Leu Gly Cys Phe Ala Val Arg Asp Met Arg Gln Thr  
355 360 365

Val Ala Val Gly Val Ile Lys Ala Val Asp Lys Lys Ala Gly Ala  
370 375 380

Gly Lys Val Thr Lys Ser Ala Gln Lys Ala Gln Lys Ala Lys  
385 390 395

<210> 177  
<211> 334  
<212> PRT  
<213> Homo sapiens  
<400> 177

Met Ala Thr Leu Lys Glu Lys Leu Ile Ala Pro Val Ala Glu Glu Glu  
1 5 10 15

Ala Thr Val Pro Asn Asn Lys Ile Thr Val Val Gly Val Gly Gln Val  
20 30

Gly Met Ala Cys Ala Ile Ser Ile Leu Gly Lys Ser Leu Ala Asp Glu  
33 40 45

Leu Ala Leu Val Asp Val Leu Glu Asp Lys Leu Lys Gly Glu Met Met  
50 55 60

Asp Leu Gln His Gly Ser Leu Phe Leu Gln Thr Pro Lys Ile Val Ala  
65 70 75 80

Asp Lys Asp Tyr Ser Val Thr Ala Asn Ser Lys Ile Val Val Thr  
85 90 95

Ala Gly Val Arg Gln Gln Gly Glu Ser Arg Leu Asn Leu Val Gln  
100 105 110

Arg Asn Val Asn Val Phe Lys Phe Ile Ile Pro Gln Ile Val Lys Tyr  
115 120 125

Ser Pro Asp Cys Ile Ile Ile Val Val Ser Asn Pro Val Asp Ile Leu  
130 135 140

Thr Tyr Val Thr Trp Lys Leu Ser Gly Leu Pro Lys His Arg Val Ile  
145 150 155

Gly Ser Gly Cys Asn Leu Asp Ser Ala Arg Phe Arg Tyr Leu Met Ala  
160 165 170 175

Glu Lys Leu Gly Ile His Pro Ser Ser Cys His Gly Trp Ile Leu Gly  
180 185 190

Glu His Gly Asp Ser Ser Val Ala Val Trp Ser Gly Val Asn Val Ala  
195 200 205

Gly Val Ser Leu Gln Glu Leu Asn Pro Glu Met Gly Thr Asp Asn Asp  
210 215 220

Ser Glu Asn Trp Lys Glu Val His Lys Met Val Val Glu Ser Ala Tyr  
225 230 235 240

Glu Val Ile Lys Leu Lys Gly Tyr Thr Asn Trp Ala Ile Gly Leu Ser  
245 250 255

Val Ala Asp Leu Ile Glu Ser Met Leu Lys Asn Leu Ser Arg Ile His  
260 265 270

Pro Val Ser Thr Met Val Lys Gly Met Tyr Gly Ile Glu Asn Glu Val  
275 280 285

Phe Leu Ser Leu Pro Cys Ile Leu Asn Ala Arg Gly Leu Thr Ser Val  
290 295 300

Ile Asn Gln Lys Leu Lys Asp Asp Glu Val Ala Gln Leu Lys Lys Ser  
305 310 315 320

Ala Asp Thr Leu Trp Asp Ile Gln Lys Asp Leu Lys Asp Leu  
325 330

<210> 178  
<211> 364  
<212> PRT  
<213> Homo sapiens

<400> 178

Met Tyr Leu Ser Arg Phe Leu Ser Ile His Ala Leu Trp Val Thr Val  
1 5 10 15

Ser Ser Val Met Gln Pro Tyr Pro Leu Val Trp Gly His Tyr Asp Leu  
20 25 30

Cys Lys Thr Gln Ile Tyr Thr Glu Gly Lys Val Trp Asp Tyr Met  
35 40 45

Ala Cys Gln Pro Glu Ser Thr Asp Met Thr Lys Tyr Leu Lys Val Lys  
50 55 60

Leu Asp Pro Pro Asp Ile Thr Cys Gly Asp Pro Pro Glu Thr Phe Cys  
65 70 75 80

Ala Met Gly Asn Pro Tyr Met Cys Asn Asn Glu Cys Asp Ala Ser Thr  
85 90 95

Pro Glu Leu Ala His Pro Pro Glu Leu Met Phe Asp Phe Glu Gly Arg  
100 105 110

His Pro Ser Thr Phe Trp Gln Ser Ala Thr Trp Lys Glu Tyr Pro Lys  
115 120 125

Pro Leu Gln Val Asn Ile Thr Leu Ser Trp Ser Lys Thr Ile Glu Leu  
130 135 140

Thr Asp Asn Ile Val Ile Thr Phe Glu Ser Gly Arg Pro Asp Gln Met  
145 150 155 160

Ile Leu Glu Lys Ser Leu Asp Tyr Gly Arg Thr Trp Gln Pro Tyr Gln  
165 170 175

Tyr Tyr Ala Thr Asp Cys Leu Asp Ala Phe His Met Asp Pro Lys Ser  
180 185 190

Val Lys Asp Leu Ser Gln His Thr Val Leu Glu Ile Ile Cys Thr Glu  
195 200 205

Glu Tyr Ser Thr Gly Tyr Thr Thr Asn Ser Lys Ile Ile His Phe Glu  
210 215 220

Ile Lys Asp Arg Phe Ala Phe Phe Ala Gly Pro Arg Leu Arg Asn Met  
225 230 235 240

Ala Ser Leu Tyr Gly Gln Leu Asp Thr Thr Lys Lys Leu Arg Asp Phe  
245 250 255

Phe Thr Val Thr Asp Leu Arg Ile Arg Leu Leu Arg Pro Ala Val Gly  
260 265 270

Glu Ile Phe Val Asp Glu Leu His Leu Ala Arg Tyr Phe Tyr Ala Ile  
275 280 285

Ser Asp Ile Lys Val Arg Gly Arg Cys Lys Cys Asn Leu His Ala Thr  
290 295 300

Val Cys Val Tyr Asp Asn Ser Lys Leu Thr Cys Glu Cys Glu His Asn  
305 310 315 320

Thr Thr Gly Pro Asp Cys Gly Lys Cys Lys Lys Asn Tyr Gln Gly Arg  
325 330 335

Pro Trp Ser Pro Gly Ser Tyr Leu Pro Ile Pro Lys Gly Thr Ala Asn  
340 345 350

Thr Cys Ile Pro Ser Ile Ser Ser Ile Gly Ser Lys  
355 360

<210> 179  
<211> 416  
<212> PRT  
<213> Homo sapiens

<400> 179

Met His Thr Asp Pro Asp Tyr Ser Ala Ala Tyr Val Val Ile Glu Thr  
1 5 10 15

Asp Ala Glu Asp Gly Ile Lys Gly Cys Gly Ile Thr Phe Thr Leu Gly  
20 25 30

Lys Gly Thr Glu Val Val Cys Ala Val Asn Ala Leu Ala His His  
35 40 45

Val Leu Asn Lys Asp Leu Lys Asp Ile Val Gly Asp Phe Arg Gly Phe  
50 55 60

Tyr Arg Gln Leu Thr Ser Asp Gly Gln Leu Arg Trp Ile Gly Pro Glu  
65 70 75 80

Lys Gly Val Val His Leu Ala Thr Ala Ala Val Leu Asn Ala Val Trp  
85 90 95

Asp Leu Trp Ala Lys Gln Glu Gly Lys Pro Val Trp Lys Leu Leu Val  
100 105 110

Asp Met Asp Pro Arg Met Leu Val Ser Cys Ile Asp Phe Arg Tyr Ile  
115 120 125

Thr Asp Val Leu Thr Glu Glu Asp Ala Leu Glu Ile Leu Gln Lys Gly  
130 135 140

Gln Ile Gly Lys Lys Glu Arg Glu Lys Gln Met Leu Ala Gln Gly Tyr  
145 150 155 160

Pro Ala Tyr Thr Ser Cys Ala Trp Leu Gly Tyr Ser Asp Asp Thr  
165 170 175

Leu Lys Gln Leu Cys Ala Gln Ala Leu Lys Asp Gly Trp Thr Arg Phe  
180 185 190

Lys Val Lys Val Gly Ala Asp Leu Gln Asp Met Arg Arg Cys Gln  
195 200 205 210

Ile Ile Arg Asp Met Ile Gly Pro Glu Lys Thr Leu Met Met Asp Ala  
210 215 220

Asn Gln Arg Trp Asp Val Pro Glu Ala Val Glu Trp Met Ser Lys Leu  
225 230 235 240

Ala Lys Phe Lys Pro Leu Trp Ile Glu Glu Pro Thr Ser Pro Asp Asp  
245 250 255

Ile Leu Gly His Ala Thr Ile Ser Lys Ala Leu Val Pro Leu Gly Ile  
260 265 270

Gly Ile Ala Thr Gly Glu Gln Cys His Asn Arg Val Ile Phe Lys Gln  
275 280 285

Leu Leu Gln Ala Lys Ala Leu Gln Phe Leu Gln Ile Asp Ser Cys Arg  
290 295 300

Leu Gly Ser Val Asn Glu Asn Leu Ser Val Leu Leu Met Ala Lys Lys  
305 310 315 320

Phe Glu Ile Pro Val Cys Pro His Ala Gly Gly Val Gly Leu Cys Glu  
325 330 335

Leu Val Gln His Leu Ile Ile Phe Asp Tyr Ile Ser Val Ser Ala Ser  
340 345 350

Leu Glu Asn Arg Val Cys Glu Tyr Val Asp His Leu His Glu His Phe  
355 360 365

Lys Tyr Pro Val Met Ile Gln Arg Ala Ser Tyr Met Pro Pro Lys Asp  
370 375 380

Pro Gly Tyr Ser Thr Glu Met Lys Glu Glu Ser Val Lys Lys His Gln  
385 390 395 400

Tyr Pro Asp Gly Glu Val Trp Lys Lys Leu Leu Pro Ala Gln Glu Asn  
405 410 415

<210> 180  
<211> 89  
<212> PRT  
<213> Homo sapiens

<400> 180

Met Ser Ser Gln Gln Gln Lys Gln Pro Cys Ile Pro Pro Pro Gln Leu  
1 5 10 15

Gln Gln Gln Gln Val Lys Gln Pro Cys Gln Pro Pro Pro Gln Glu Pro  
20 25 30

Cys Ile Pro Lys Thr Lys Glu Pro Cys His Pro Lys Val Pro Glu Pro  
35 40 45

Cys His Pro Lys Val Pro Glu Pro Cys Gln Pro Lys Leu Pro Glu Pro  
50 55 60

Cys His Pro Lys Val Pro Glu Pro Cys Pro Ser Ile Val Thr Pro Ala  
65 70 75 80

Pro Ala Gln Gln Lys Thr Lys Gln Lys 85	
<210> 181	<212> PRT
<211> 233	<213> Homo sapiens
<212> PRT	
<213> Homo sapiens	
<400> 181	<400> 182
Met Ala Arg Ser Leu Leu Leu Pro Leu Gln Ile Leu Leu Leu Ser Leu 1 5 10 15	Met Leu Ala Thr Arg Val Phe Ser Leu Val Gly Lys Arg Ala Ile Ser 1 5 10 15
Ala Leu Gln Thr Ala Gly Gln Gln Ala Gln Gly Asp Lys Ile Ile Asp 20 25 30	Thr Ser Val Cys Val Arg Ala His Gln Ser Val Val Lys Ser Gln Asp 20 25 30
Gly Ala Pro Cys Ala Arg Gly Ser His Pro Trp Gln Val Ala Leu Leu 35 40 45	Phe Ser Leu Pro Ala Tyr Met Asp Arg Asp His Pro Leu Pro Gln 35 40 45
Ser Gly Asn Gln Leu His Cys Gly Gly Val Leu Val Asn Gln Arg Trp 50 55 60	Val Ala His Val Lys His Leu Ser Ala Ser Gln Lys Ala Leu Lys Gln 50 55 60
Val Leu Thr Ala Ala His Cys Lys Met Asn Gln Tyr Thr Val His Leu 65 70 75	Lys Gln Lys Ala Ser Trp Ser Ser Leu Ser Met Asp Gln Lys Val Gln 65 70 75
Gly Ser Asp Thr Leu Gly Asp Arg Arg Ala Gln Arg Ile Lys Ala Ser 85 90 95	Leu Tyr Arg Ile Lys Phe Lys Gln Ser Phe Ala Gln Met Asn Arg Gly 85 90 95
Lys Ser Phe Arg His Pro Gly Tyr Ser Thr Gln Thr His Val Asn Asp 100 105 110	Ser Asn Gln Trp Lys Thr Val Val Gly Gln Ala Met Phe Phe Ile Gly 100 105 110
Leu Met Leu Val Lys Leu Asn Ser Gln Ala Arg Leu Ser Ser Met Val 115 120 125	Phe Thr Ala Leu Val Ile Met Trp Gln Lys His Tyr Val Tyr Gly Pro 115 120 125
Lys Lys Val Arg Leu Pro Ser Arg Cys Gln Pro Pro Gly Thr Thr Cys 130 135 140	Leu Pro Gln Ser Phe Asp Lys Gln Trp Val Ala Lys Gln Thr Lys Arg 130 135 140
Thr Val Ser Gly Trp Gly Thr Thr Thr Ser Pro Asp Val Thr Phe Pro 145 150 155	Met Leu Asp Met Lys Val Asn Pro Ile Gln Gly Leu Ala Ser Lys Trp 145 150 155
Ser Asp Leu Met Cys Val Asp Val Lys Leu Ile Ser Pro Gln Asp Cys 165 170 175	Asp Tyr Gln Lys Asn Gln Trp Lys Lys 165
Thr Lys Val Tyr Lys Asp Leu Leu Gln Asn Ser Met Leu Cys Ala Gly 180 185 190	<210> 183
Ile Pro Asp Ser Lys Lys Asn Ala Cys Asn Gly Asp Ser Gly Gly Pro 195 200 205	<211> 879
Leu Val Cys Arg Gly Thr Leu Gln Gly Leu Val Ser Trp Gly Thr Phe 210 215 220	<212> PRT
Pro Cys Gly Gln Pro Asn Asp Pro Gly Val Tyr Thr Gln Val Cys Lys 225 230 235	<213> Homo sapiens
Phe Thr Lys Trp Ile Asn Asp Thr Met Lys Lys His Arg 240 245 250	<400> 183
<210> 182	Met Ala Gly Gly Gly Asp Leu Ser Thr Arg Arg Leu Asn Gln Cys 1 5 10 15
<211> 169	Ile Ser Pro Val Ala Asn Gln Met Asn His Leu Pro Ala His Ser His 20 25 30
	Asp Leu Gln Arg Met Phe Thr Gln Asp Gln Gly Val Asp Asp Arg Leu 35 40 45
	Leu Tyr Asp Ile Val Phe Lys His Phe Lys Arg Asn Lys Val Gln Ile 50 55 60
	Ser Asn Ala Ile Lys Lys Thr Phe Pro Phe Leu Gln Gly Leu Arg Asp 65 70 75
	Arg Asp Leu Ile Thr Asn Lys Met Phe Gln Asp Ser Gln Asp Ser Cys 85 90 95

Arg Asn Leu Val Pro Val Gln Arg Val Val Tyr Asn Val Leu Ser Glu 100 105 110  
Leu Glu Lys Thr Phe Asn Leu Pro Val Leu Glu Ala Leu Phe Ser Asp 115 120 125  
Val Asn Met Gln Glu Tyr Pro Asp Leu Ile His Ile Tyr Lys Gly Phe 130 135 140 145  
Glu Asn Val Ile His Asp Lys Leu Pro Leu Gln Glu Ser Glu Glu Glu 145 150 155 160  
Glu Arg Glu Glu Arg Ser Gly Leu Gln Leu Ser Leu Glu Gln Gly Thr 165 170 175  
Gly Glu Asn Ser Phe Arg Ser Leu Thr Trp Pro Pro Ser Gly Ser Pro 180 185 190  
Ser His Ala Gly Thr Thr Pro Pro Glu Asn Gly Leu Ser Glu His Pro 195 200 205  
Cys Glu Thr Glu Gln Ile Asn Ala Lys Arg Lys Asp Thr Thr Ser Asp 210 215 220  
Lys Asp Asp Ser Leu Gly Ser Gln Gln Thr Asn Glu Gln Cys Ala Gln 225 230 235 240  
Lys Ala Glu Pro Thr Glu Ser Cys Glu Gln Ile Ala Val Gln Val Asn 245 250 255  
Asn Gly Asp Ala Gly Arg Glu Met Pro Cys Pro Leu Pro Cys Asp Glu 260 265 270  
Glu Ser Pro Glu Ala Glu Leu His Asn His Gly Ile Gln Ile Asn Ser 275 280 285  
Cys Ser Val Arg Leu Val Asp Ile Lys Lys Glu Lys Pro Phe Ser Asn 290 295 300  
Ser Lys Val Glu Cys Gln Ala Gln Ala Arg Thr His His Asn Gln Ala 305 310 315 320  
Ser Asp Ile Ile Val Ile Ser Ser Glu Asp Ser Glu Gly Ser Thr Asp 325 330 335  
Val Asp Glu Pro Leu Glu Val Phe Ile Ser Ala Pro Arg Ser Glu Pro 340 345 350  
Val Ile Asn Asn Asp Asn Pro Leu Glu Ser Asn Asp Glu Lys Glu Gly 355 360 365  
Gln Glu Ala Thr Cys Ser Arg Pro Gln Ile Val Pro Glu Pro Met Asp 370 375 380  
Phe Arg Lys Leu Ser Thr Phe Arg Glu Ser Phe Lys Lys Arg Val Ile 385 390 395  
Gly Gln Asp His Asp Phe Ser Glu Ser Ser Glu Glu Glu Ala Pro Ala 405 410 415

Glu Ala Ser Ser Gly Ala Leu Arg Ser Lys His Gly Glu Lys Ala Pro 420 425 430  
Met Thr Ser Arg Ser Thr Ser Thr Trp Arg Ile Pro Ser Arg Lys Arg 435 440 445  
Arg Phe Ser Ser Ser Asp Phe Ser Asp Leu Ser Asn Gly Glu Glu Leu 450 455 460  
Gln Glu Thr Cys Ser Ser Ser Leu Arg Arg Gly Ser Gly Ser Gln Pro 465 470 475 480  
Gln Glu Pro Glu Asn Lys Lys Cys Ser Cys Val Met Cys Phe Pro Lys 485 490 495  
Gly Val Pro Arg Ser Gln Glu Ala Arg Thr Glu Ser Ser Gln Ala Ser 500 505 510  
Asp Met Met Asp Thr Met Asp Val Glu Asn Asn Ser Thr Leu Glu Lys 515 520 525  
His Ser Gly Lys Arg Arg Lys Lys Arg His Arg Ser Lys Val Asn 530 535 540  
Gly Leu Gln Arg Gly Arg Lys Lys Asp Arg Pro Arg Lys His Leu Thr 545 550 555 560  
Leu Asn Asn Lys Val Gln Lys Lys Arg Trp Gln Gln Arg Gly Arg Lys 565 570 575  
Ala Asn Thr Arg Pro Leu Lys Arg Arg Arg Lys Arg Gly Pro Arg Ile 580 585 590  
Pro Lys Asp Glu Asn Ile Asn Phe Lys Gln Ser Glu Leu Pro Val Thr 595 600 605  
Cys Gly Glu Val Lys Gly Thr Leu Tyr Lys Glu Arg Phe Lys Gln Gly 610 615 620  
Thr Ser Lys Lys Cys Ile Gln Ser Glu Asp Lys Lys Trp Phe Thr Pro 625 630 635 640  
Arg Glu Phe Glu Ile Glu Gly Asp Arg Gly Ala Ser Lys Asn Trp Lys 645 650 655  
Leu Ser Ile Arg Cys Gly Gly Tyr Thr Leu Lys Val Leu Met Glu Asn 660 665 670  
Lys Phe Leu Pro Glu Pro Pro Ser Thr Arg Lys Lys Arg Ile Leu Glu 675 680 685  
Ser His Asn Asn Thr Leu Val Asp Pro Cys Glu His Lys Lys Lys 690 695 700  
Asn Pro Asp Ala Ser Val Lys Phe Ser Glu Phe Leu Lys Lys Cys Ser 705 710 715 720  
Glu Thr Trp Lys Thr Ile Phe Ala Lys Glu Lys Gly Lys Phe Glu Asp 405 410 415

725 730 735

Met Ala Lys Ala Asp Lys Ala His Tyr Glu Arg Glu Met Lys Thr Tyr  
740 745 750

Ile Pro Pro Lys Gly Glu Lys Lys Lys Phe Lys Asp Pro Asn Ala  
755 760 765

Pro Lys Arg Pro Pro Leu Ala Phe Phe Leu Phe Cys Ser Glu Tyr Arg  
770 775 780

Pro Lys Ile Lys Gly Glu His Pro Gly Leu Ser Ile Asp Asp Val  
785 790 795 800

Lys Lys Leu Ala Gly Met Trp Asn Asn Thr Ala Ala Ala Asp Lys Gln  
805 810 815

Phe Tyr Glu Lys Lys Ala Ala Lys Ileu Lys Glu Lys Tyr Lys Lys Asp  
820 825 830

Ile Ala Ala Tyr Arg Ala Lys Gly Lys Pro Asn Ser Ala Lys Lys Arg  
835 840 845

Val Val Lys Ala Glu Lys Ser Lys Lys Lys Glu Glu Glu Glu Asp  
850 855 860

Glu Glu Asp Glu Gln Glu Glu Asn Glu Asp Asp Lys  
865 870 875

<210> 104  
<211> 316  
<212> PRT  
<213> Homo sapiens  
<400> 184

Met Ala Ser Thr Ser Arg Leu Asp Ala Leu Pro Arg Val Thr Cys Pro  
1 5 10 15

Asn His Pro Asp Ala Ile Leu Val Glu Asp Tyr Arg Ala Gly Asp Met  
20 25 30

Ile Cys Pro Glu Cys Gly Leu Val Val Gly Asp Arg Val Ile Asp Val  
35 40 45

Gly Ser Glu Trp Arg Thr Phe Ser Asn Asp Lys Ala Thr Lys Asp Pro  
50 55 60

Ser Arg Val Gly Asp Ser Gln Asn Pro Leu Leu Ser Asp Gly Asp Leu  
65 70 75 80

Ser Thr Met Ile Gly Lys Gly Thr Gly Ala Ala Ser Phe Asp Glu Phe  
85 90 95

Gly Asn Ser Lys Tyr Gln Asn Arg Thr Met Ser Ser Ser Asp Arg  
100 105 110

Ala Met Met Asn Ala Phe Lys Glu Ile Thr Thr Met Ala Asp Arg Ile  
115 120 125

Asn Leu Pro Arg Asn Ile Val Asp Arg Thr Asn Asn Leu Phe Lys Gln

130 135 140

Val Tyr Glu Gln Lys Ser Leu Lys Gly Arg Ala Asn Asp Ala Ile Ala  
145 150 155 160

Ser Ala Cys Leu Tyr Ile Ala Cys Arg Gln Glu Gly Val Pro Arg Thr  
165 170 175

Phe Lys Glu Ile Cys Ala Val Ser Arg Ile Ser Lys Lys Glu Ile Gly  
180 185 190

Arg Cys Phe Lys Leu Ile Leu Lys Ala Leu Glu Thr Ser Val Asp Leu  
195 200 205

Ile Thr Thr Gly Asp Phe Met Ser Arg Phe Cys Ser Asn Leu Cys Leu  
210 215 220

Pro Lys Gln Val Gln Met Ala Ala Thr His Ile Ala Arg Lys Ala Val  
225 230 235 240

Glu Leu Asp Leu Val Pro Gly Arg Ser Pro Ile Ser Val Ala Ala Ala  
245 250 255

Ala Ile Tyr Met Ala Ser Gln Ala Ser Ala Glu Lys Arg Thr Gln Lys  
260 265 270

Glu Ile Gly Asp Ile Ala Gly Val Ala Asp Val Thr Ile Arg Gln Ser  
275 280 285

Tyr Arg Leu Ile Tyr Pro Arg Ala Pro Asp Leu Phe Pro Thr Asp Phe  
290 295 300

Lys Phe Asp Thr Pro Val Asp Lys Leu Pro Gln Leu  
305 310 315

<210> 185  
<211> 628  
<212> PRT  
<213> Homo sapiens  
<400> 185

Ala Asp Phe Leu Asp Ala Leu Ile Val Ser Met Asp Val Ile Gln His  
1 5 10 15

Glu Thr Ile Gly Lys Lys Phe Glu Lys Arg His Ile Glu Ile Phe Thr  
20 25 30

Asp Leu Ser Ser Arg Phe Ser Lys Ser Gln Leu Asp Ile Ile Ile His  
35 40 45

Ser Leu Lys Lys Cys Asp Ile Ser Leu Gln Phe Phe Leu Pro Phe Ser  
50 55 60

Leu Gly Lys Glu Asp Gly Ser Gly Asp Arg Gly Asp Gly Pro Phe Arg  
65 70 75 80

Leu Gly Gly His Gly Pro Ser Phe Pro Leu Lys Gly Ile Thr Glu Gln  
85 90 95

Gln Lys Glu Gly Leu Glu Ile Val Lys Met Val Met Ile Ser Leu Glu

100 105 110  
 Gly Glu Asp Gly Leu Asp Glu Ile Tyr Ser Phe Ser Glu Ser Leu Arg  
 115 120 125  
 Lys Leu Cys Val Phe Lys Lys Ile Glu Arg His Ser Ile His Trp Pro  
 130 135 140  
 Cys Arg Leu Thr Ile Gly Ser Asn Leu Ser Ile Arg Ile Ala Ala Tyr  
 145 150 155 160  
 Lys Ser Ile Leu Glu Glu Arg Val Lys Lys Thr Trp Thr Val Val Asp  
 165 170 175  
 Ala Lys Thr Leu Lys Lys Glu Asp Ile Glu Lys Glu Thr Val Tyr Cys  
 180 185 190  
 Leu Asn Asp Asp Asp Glu Thr Glu Val Leu Lys Glu Asp Ile Ile Glu  
 195 200 205  
 Gly Phe Leu Tyr Gly Ser Asp Ile Val Pro Phe Ser Lys Val Asp Glu  
 210 215 220  
 Glu Glu Met Lys Tyr Lys Ser Glu Gly Lys Cys Phe Ser Val Leu Gly  
 225 230 235  
 Phe Cys Lys Ser Ser Glu Val Glu Arg Arg Phe Phe Met Gly Asn Glu  
 240 245 250 255  
 Val Leu Lys Val Phe Ala Ala Arg Asp Asp Glu Ala Ala Val Ala  
 260 265 270  
 Leu Ser Ser Leu Ile His Ala Leu Asp Asp Leu Asp Met Val Ala Ile  
 275 280 285  
 Val Arg Tyr Ala Tyr Asp Lys Arg Ala Asn Pro Glu Val Gly Val Ala  
 290 295 300  
 Phe Pro His Ile Lys His Asn Tyr Glu Cys Leu Val Tyr Val Glu Leu  
 305 310 315 320  
 Pro Phe Met Glu Asp Leu Arg Glu Tyr Met Phe Ser Ser Leu Lys Asn  
 320 325 330 335  
 Ser Lys Lys Tyr Ala Pro Thr Glu Ala Glu Lys Asn Ala Val Asp Ala  
 340 345 350  
 Leu Ile Asp Ser Met Ser Leu Ala Lys Lys Asp Glu Lys Thr Asp Thr  
 355 360 365  
 Leu Glu Asp Leu Phe Pro Thr Thr Lys Ile Pro Asn Pro Arg Phe Glu  
 370 375 380  
 Arg Leu Phe Glu Cys Leu Leu His Arg Ala Leu His Pro Arg Glu Pro  
 385 390 395 400  
 Leu Pro Pro Ile Glu Glu His Ile Trp Asn Met Leu Asn Pro Pro Ala  
 405 410 415

Glu Val Thr Thr Lys Ser Glu Ile Pro Leu Ser Lys Ile Lys Thr Leu  
 420 425 430  
 Phe Pro Leu Ile Glu Ala Lys Lys Lys Asp Glu Val Thr Ala Glu Glu  
 435 440 445  
 Ile Phe Glu Asp Asn His Glu Asp Gly Pro Thr Ala Lys Lys Leu Lys  
 450 455 460  
 Thr Glu Glu Gly Gly Ala His Phe Ser Val Ser Ser Leu Ala Glu Gly  
 465 470 475 480  
 Ser Val Thr Ser Val Gly Ser Val Asn Pro Ala Glu Asn Phe Arg Val  
 485 490 495  
 Leu Val Lys Glu Lys Lys Ala Ser Phe Glu Glu Ala Ser Asn Glu Leu  
 500 505 510  
 Ile Asn His Ile Glu Glu Phe Leu Asp Thr Asn Glu Thr Pro Tyr Phe  
 515 520 525  
 Met Lys Ser Ile Asp Cys Ile Arg Ala Phe Arg Glu Glu Ala Ile Lys  
 530 535 540  
 Phe Ser Glu Glu Glu Arg Phe Asn Asn Phe Leu Lys Ala Leu Glu Glu  
 545 550 555 560  
 Lys Val Glu Ile Lys Glu Leu Asn His Phe Trp Glu Ile Val Val Glu  
 565 570 575  
 Asp Gly Ile Thr Leu Ile Thr Lys Glu Glu Ala Ser Gly Ser Ser Val  
 580 585 590  
 Thr Ala Glu Glu Ala Lys Lys Phe Leu Ala Pro Lys Asp Lys Pro Ser  
 595 600 605  
 Gly Asp Thr Ala Ala Val Phe Glu Glu Gly Asp Val Asp Asp Leu  
 610 615 620  
 Leu Asp Met Ile  
 625  
 <210> 186  
 <211> 420  
 <212> PRT  
 <213> Homo sapiens  
 <400> 186  
 Met Gly Ser Gly Trp Lys Lys Ile Lys Leu Glu Met Lys Cys Asp Gly  
 1 10 15  
 Cys Ser Glu Glu Gly Ser His Pro Cys Ala Phe Ile Gly Ile Gly Asn  
 20 25 30  
 Ser Asp Glu Glu Met Glu Glu Asn Leu Glu Gly Lys Asn Tyr Cys  
 35 40 45  
 Thr Ala Lys Thr Leu Tyr Ile Ser Asp Ser Asp Lys Glu Lys His Phe  
 50 55 60

Met Leu Ser Val Lys Val Phe Tyr Gly Asp Asp Ile Gly Val 80  
65 75

Phe Leu Ser Lys Ser Lys Pro Ser Lys Lys Lys Gln Ser Leu Lys 95  
85

Asn Ala Asp Leu Cys Ile Gly Ser Gly Thr Lys Val Ala Leu Phe Asn 110  
100 105

Arg Leu Arg Ser Gln Thr Val Ser Thr Arg Tyr Leu His Val Glu Gly 125  
115 120

Gly Asn Phe His Ala Ser Ser Gln Gln Trp Gly Ala Phe Thr Leu Phe 140  
130 135

Leu Asp Asp Asp Gly Ser Glu Gly Glu Phe Thr Val Arg Asp Gly 160  
145 150 155

Tyr Ile His Tyr Gly Gln Thr Val Lys Leu Val Cys Ser Val Thr Gly 175  
165 170

Met Ala Leu Pro Arg Leu Ile Ile Arg Lys Val Asp Lys Gln Thr Thr 190  
180 185

Leu Leu Asp Ala Asp Asp Pro Val Ser Gln Leu His Lys Cys Ala Phe 205  
195 200

Asp Leu Glu Asp Thr Glu Arg Met Tyr Leu Cys Leu Ser Gln Glu Arg 220  
210 215

Ile Ile Gln Phe Gln Ala Thr Pro Cys Pro Thr Glu Pro Asn Lys Glu 240  
225 230 235

Met Ile Asn Asp Gly Ala Ser Trp Ala Ile Ile Ser Thr His Lys Ala 255  
245 250

Lys Tyr Thr Phe Tyr Glu Arg Met Gly Pro Val Leu Ala Leu Val Met 270  
260 265

Pro Met Pro Val Val Glu Ser Leu Lys Leu Asn Gly Gly Asp Gln 285  
275 280

Ala Met Leu Glu Leu Thr Gly Gln Asn Phe Thr Pro Asn Leu Arg Val 300  
290 295

Trp Phe Gly Asp Val Glu Ala Glu Thr Met Tyr Arg Cys Gly Glu Ser 320  
305 310 315

Met Leu Arg Val Val Pro Asp Val Leu His Ser Glu Lys Val Gly Asp 335  
325 330

Ser Ser Gln Gln Pro Val Gln Val Ser Val Thr Leu Val Arg Asn Asp 350  
340 345

Gly Ile Ile Tyr Ser Thr Ser Leu Thr Phe Thr Tyr Thr Pro Glu Ala 365  
355 360

Gly Pro Arg Pro His Cys Ser Val Ala Gly Ala Ile Leu Lys Ala Ser 380  
370 375

Ser Ser His Val Pro Pro Asn Glu Leu Asn Thr Asn Ser Asp Gly Ser 400  
385 390 395

Tyr Thr Asn Ala Ser Thr Asn Ser Thr Ser Val Thr Ser Ser Thr Pro 415  
405 410

Thr Val Val Ser 420

<210> 187  
<211> 103  
<212> PRT  
<213> Homo sapiens  
<400> 187

Met Glu Thr Val Gln Glu Leu Ile Pro Leu Ala Lys Glu Met Met Ala 15  
1 5 10

Gln Lys Arg Lys Gly Lys Met Val Lys Leu Tyr Val Leu Gly Ser Val 30  
20 25

Leu Ala Leu Phe Gly Val Val Leu Gly Leu Met Glu Thr Val Cys Ser 45  
35 40

Pro Phe Thr Ala Ala Arg Arg Leu Arg Asp Gln Glu Ala Ala Val Ala 60  
50 55

Glu Leu Gln Ala Ala Leu Glu Arg Gln Ala Leu Gln Lys Gln Ala Leu 80  
65 70 75

Gln Glu Lys Gly Lys Gln Gln Asp Thr Val Leu Gly Gly Arg Ala Leu 95  
85 90

Ser Asn Arg Gln His Ala Ser 100

<210> 188  
<211> 1306  
<212> PRT  
<213> Homo sapiens  
<400> 188

Met Gly Ala Ala Ser Gly Arg Arg Gly Pro Gly Leu Leu Leu Pro Leu 15  
1 5 10

Pro Leu Leu Leu Leu Leu Pro Gln Pro Ala Leu Ala Leu Asp Pro 30  
20 25

Gly Leu Gln Pro Gly Asn Phe Ser Ala Asp Glu Ala Gly Ala Gln Leu 45  
35 40

Phe Ala Gln Ser Tyr Asn Ser Ser Ala Glu Gln Val Leu Phe Gln Ser 60  
50 55

Val Ala Ala Ser Trp Ala His Asp Thr Asn Ile Thr Ala Glu Asn Ala 80  
65 70 75

Arg Arg Gln Glu Glu Ala Ala Leu Leu Ser Gln Glu Phe Ala Glu Ala 95  
85 90



Trp Gly Gln Lys Ala Lys Lys Glu Leu Tyr Gln Pro Ile Trp Gln Asn Phe  
 100 110  
 Thr Asp Pro Gln Leu Arg Arg Ile Ile Gly Ala Val Arg Thr Leu Gly  
 115 120 125  
 Ser Ala Asn Leu Pro Leu Ala Lys Arg Gln Gln Tyr Asn Ala Leu Leu  
 130 135 140  
 Ser Asn Met Ser Arg Ile Tyr Ser Thr Ala Lys Val Cys Leu Pro Asn  
 145 150 155 160  
 Lys Thr Ala Thr Cys Trp Ser Leu Asp Pro Asp Leu Thr Asn Ile Leu  
 165 170 175  
 Ala Ser Ser Arg Ser Tyr Ala Met Leu Leu Phe Ala Trp Glu Gly Trp  
 180 185 190  
 His Asn Ala Ala Gly Ile Pro Leu Lys Pro Leu Tyr Glu Asp Phe Thr  
 195 200 205  
 Ala Leu Ser Asn Glu Ala Tyr Lys Lys Gln Asp Gly Phe Thr Asp Thr Gly  
 210 215 220  
 Ala Tyr Trp Arg Ser Trp Tyr Asn Ser Pro Thr Phe Glu Asp Asp Leu  
 225 230 235  
 Glu His Leu Tyr Gln Gln Leu Glu Pro Leu Tyr Leu Asn Leu His Ala  
 240 245 250  
 Phe Val Arg Arg Ala Leu His Arg Arg Tyr Gly Asp Arg Tyr Ile Asn  
 255 260 265 270  
 Leu Arg Gly Pro Ile Pro Ala His Leu Leu Gly Asp Met Trp Ala Gln  
 275 280 285  
 Ser Trp Glu Asn Ile Tyr Asp Met Val Val Pro Phe Pro Asp Lys Pro  
 290 295 300  
 Asn Leu Asp Val Thr Ser Thr Met Leu Gln Gln Gly Trp Asn Ala Thr  
 305 310 315 320  
 His Met Phe Arg Val Ala Glu Glu Phe Thr Ser Leu Glu Leu Ser  
 325 330 335  
 Pro Met Pro Pro Glu Phe Trp Glu Gly Ser Met Leu Glu Lys Pro Ala  
 340 345 350  
 Asp Gly Arg Glu Val Val Cys His Ala Ser Ala Trp Asp Phe Tyr Asn  
 355 360 365  
 Arg Lys Asp Phe Arg Ile Lys Gln Cys Thr Arg Val Thr Met Asp Gln  
 370 375 380  
 Leu Ser Thr Val His His Glu Met Gly His Ile Gln Tyr Tyr Leu Gln  
 385 390 395 400  
 Tyr Lys Asp Leu Pro Val Ser Leu Arg Arg Gly Ala Asn Pro Gly Phe  
 405 410 415

His Glu Ala Ile Gly Asp Val Leu Ala Leu Ser Val Ser Thr Pro Glu  
 420 425 430  
 His Leu His Lys Ile Gly Leu Leu Asp Arg Val Thr Asn Asp Thr Glu  
 435 440 445  
 Ser Asp Ile Asn Tyr Leu Leu Lys Met Ala Leu Glu Lys Ile Ala Phe  
 450 455 460  
 Leu Pro Phe Gly Tyr Leu Val Asp Gln Trp Arg Trp Gly Val Phe Ser  
 465 470 475 480  
 Gly Arg Thr Pro Pro Ser Arg Tyr Asn Phe Asp Trp Tyr Leu Arg  
 485 490 495  
 Thr Lys Tyr Gln Gly Ile Cys Pro Pro Val Thr Arg Asn Glu Thr His  
 500 505 510  
 Phe Asp Ala Gly Ala Lys Phe His Val Pro Asn Val Thr Pro Tyr Ile  
 515 520 525  
 Arg Tyr Phe Val Ser Phe Val Leu Gln Phe His Glu Ala Leu  
 530 535 540  
 Cys Lys Glu Ala Gly Tyr Glu Gly Pro Leu His Gln Cys Asp Ile Tyr  
 545 550 555 560  
 Arg Ser Thr Lys Ala Gly Ala Lys Leu Arg Lys Val Leu Gln Ala Gly  
 565 570 575  
 Ser Ser Arg Pro Trp Gln Glu Val Leu Lys Asp Met Val Gly Leu Asp  
 580 585 590  
 Ala Leu Asp Ala Gln Pro Leu Leu Lys Tyr Phe Gln Pro Val Thr Gln  
 595 600 605  
 Trp Leu Gln Glu Gln Asn Gln Asn Gly Glu Val Leu Gly Trp Pro  
 610 615 620  
 Glu Tyr Gln Trp His Pro Pro Leu Pro Asp Asn Tyr Pro Glu Gly Ile  
 625 630 635 640  
 Asp Leu Val Thr Asp Glu Ala Glu Ala Ser Lys Phe Val Glu Glu Tyr  
 645 650 655  
 Asp Arg Thr Ser Gln Val Val Trp Asn Glu Tyr Ala Glu Ala Asn Trp  
 660 665 670  
 Asn Tyr Asn Thr Asn Ile Thr Thr Glu Thr Ser Lys Ile Leu Leu Gln  
 675 680 685  
 Lys Asn Met Gln Ile Ala Asn His Thr Leu Lys Tyr Gly Thr Gln Ala  
 690 695 700  
 Arg Lys Phe Asp Val Asn Gln Leu Gln Asn Thr Thr Ile Lys Arg Ile  
 705 710 715 720  
 Ile Lys Lys Val Gln Asp Leu Glu Arg Ala Ala Leu Pro Ala Gln Glu  
 725 730 735

Leu Glu Glu Tyr Asn Lys Ile Leu Leu Asp Met Glu Thr Thr Tyr Ser  
740 745 750  
Val Ala Thr Val Cys His Pro Asn Gly Ser Cys Leu Glu Leu Glu Pro  
755 760 765  
Asp Leu Thr Asn Val Met Ala Thr Ser Arg Lys Tyr Glu Asp Leu Leu  
770 775 780  
Tyr Ala Trp Glu Gly Trp Arg Asp Lys Ala Gly Arg Ala Ile Leu Gln  
785 790 795  
Phe Tyr Pro Lys Tyr Val Glu Leu Ile Asn Gln Ala Ala Arg Leu Asn  
800 805 810  
Gly Tyr Val Asp Ala Gly Asp Ser Trp Arg Ser Met Tyr Glu Thr Pro  
820 825 830  
Ser Leu Glu Gln Asp Leu Glu Arg Leu Phe Gln Glu Leu Gln Pro Leu  
835 840 845  
Tyr Leu Asn Leu His Ala Tyr Val Arg Arg Ala Leu His Arg His Tyr  
850 855 860  
Gly Ala Gln His Ile Asn Leu Glu Gly Pro Ile Pro Ala His Leu Leu  
865 870 875  
Gly Asn Met Trp Ala Gln Thr Trp Ser Asn Ile Tyr Asp Leu Val Val  
880 885 890  
Pro Phe Pro Ser Ala Pro Ser Met Asp Thr Thr Glu Ala Met Leu Lys  
900 905 910  
Gln Gly Trp Thr Pro Arg Arg Met Phe Lys Glu Ala Asp Asp Phe Phe  
915 920 925  
Thr Ser Leu Gly Leu Leu Pro Val Pro Pro Glu Phe Trp Asn Lys Ser  
930 935 940  
Met Leu Glu Lys Pro Thr Asp Gly Arg Glu Val Val Cys His Ala Ser  
945 950 955  
Ala Trp Asp Phe Tyr Asn Gly Lys Asp Phe Arg Ile Lys Gln Cys Thr  
960 965 970 975  
Thr Val Asn Leu Glu Asp Leu Val Val Ala His His Glu Met Gly His  
980 985 990  
Ile Gln Tyr Phe Met Gln Tyr Lys Asp Leu Pro Val Ala Leu Arg Glu  
995 1000 1005  
Gly Ala Asn Pro Gly Phe His Glu Ala Ile Gly Asp Val Leu Ala  
1010 1015 1020  
Leu Ser Val Ser Thr Pro Lys His Leu His Ser Leu Asn Leu Leu  
1025 1030 1035  
Ser Ser Glu Gly Gly Ser Asp Glu His Asp Ile Asn Phe Leu Met

1040 1045 1050  
Lys Met Ala Leu Asp Lys Ile Ala Phe Ile Pro Phe Ser Tyr Leu  
1055 1060 1065  
Val Asp Gln Trp Arg Trp Arg Val Phe Asp Gly Ser Ile Thr Lys  
1070 1075 1080  
Glu Asn Tyr Asn Gln Glu Trp Trp Ser Leu Arg Leu Lys Tyr Gln  
1085 1090 1095  
Gly Leu Cys Pro Pro Val Pro Arg Thr Gln Gly Asp Phe Asp Pro  
1100 1105 1110  
Gly Ala Lys Phe His Ile Ile Pro Ser Ser Val Pro Tyr Ile Arg Tyr  
1115 1120 1125  
Phe Val Ser Phe Ile Ile Gln Phe Gln Phe His Glu Ala Leu Cys  
1130 1135 1140  
Gln Ala Ala Gly His Thr Gly Pro Leu His Lys Cys Asp Ile Tyr  
1145 1150 1155  
Gln Ser Lys Glu Ala Gly Gln Arg Leu Ala Thr Ala Met Lys Leu  
1160 1165 1170  
Gly Phe Ser Arg Pro Trp Pro Glu Ala Met Gln Leu Ile Thr Gly  
1175 1180 1185  
Gln Pro Asn Met Ser Ala Ser Ala Met Leu Ser Tyr Phe Lys Pro  
1190 1195 1200  
Leu Leu Asp Trp Leu Arg Thr Glu Asn Glu Leu His Gly Glu Lys  
1205 1210 1215  
Leu Gly Trp Pro Gln Tyr Asn Trp Thr Pro Asn Ser Ala Arg Ser  
1220 1225 1230  
Glu Gly Pro Leu Pro Asp Ser Gly Arg Val Ser Phe Leu Gly Leu  
1235 1240 1245  
Asp Leu Asp Ala Gln Gln Ala Arg Val Gly Gln Trp Leu Leu Leu  
1250 1255 1260  
Phe Leu Gly Ile Ala Leu Leu Val Ala Thr Leu Gly Leu Ser Gln  
1265 1270 1275  
Arg Leu Phe Ser Ile Arg His Arg Ser Leu His Arg His Ser His  
1280 1285 1290  
Gly Pro Gln Phe Gly Ser Glu Val Glu Leu Arg His Ser  
1295 1300 1305  
<210> 189  
<211> 1461  
<212> PRT  
<213> Homo sapiens  
<400> 189

Met Ala Ala Glu Arg Gly Ala Arg Arg Leu Leu Ser Thr Pro Ser Phe

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Trp Leu Tyr Cys Leu Leu Leu Gly Arg Arg Ala Pro Gly Ala Ala 30  
Ala Ala Arg Ser Gly Ser Ala Pro Gln Ser Pro Gly Ala Ser Ile Arg 45  
Thr Phe Thr Pro Phe Tyr Phe Leu Val Gln Pro Val Asp Thr Leu Ser 60  
Val Arg Gly Ser Ser Val Ile Leu Asn Cys Ser Ala Tyr Ser Gln Pro 80  
Ser Pro Lys Ile Gln Trp Lys Lys Asp Gly Thr Phe Leu Asn Leu Val 95  
Ser Asp Asp Arg Arg Gln Leu Leu Pro Asp Gly Ser Leu Phe Ile Ser 110  
Asn Val Val His Ser Lys His Asn Lys Pro Asp Gln Gly Tyr Tyr Gln 125  
Cys Val Ala Thr Val Gln Ser Leu Gly Thr Ile Ile Ser Arg Thr Ala 140  
Lys Leu Ile Val Ala Gly Leu Pro Arg Phe Thr Ser Gln Pro Gln Pro 160  
Ser Ser Val Tyr Ala Gly Asn Gly Ala Ile Leu Asn Cys Gln Val Asn 175  
Ala Asp Leu Val Pro Phe Val Arg Trp Gln Gln Asn Arg Gln Pro Leu 190  
Leu Leu Asp Asp Arg Val Ile Lys Leu Pro Ser Gly Met Leu Val Ile 205  
Ser Asn Ala Thr Gln Gly Asp Gly Gly Leu Tyr Arg Cys Val Val Gln 220  
Ser Gly Gly Pro Pro Lys Tyr Ser Asp Gln Val Gln Leu Lys Val Leu 240  
Pro Asp Pro Gln Val Ile Ser Asp Leu Val Phe Leu Lys Gln Pro Ser 255  
Pro Leu Val Arg Val Ile Gly Gln Asp Val Val Leu Pro Cys Val Ala 270  
Ser Gly Leu Pro Thr Pro Thr Ile Lys Trp Met Lys Asn Gln Gln Ala 285  
Leu Asp Thr Gln Ser Ser Gln Arg Leu Val Leu Leu Ala Gly Gly Ser 300  
Leu Gln Ile Ser Asp Val Thr Gln Asp Asp Ala Gly Thr Tyr Phe Cys 315  
305 310 315 320

Ile Ala Asp Asn Gly Asn Gln Thr Ile Gln Ala Gln Ala Gln Leu Thr 335  
Val Gln Ala Gln Pro Gln Phe Leu Lys Gln Pro Thr Asn Ile Tyr Ala 350  
His Gln Ser Met Asp Ile Val Phe Gln Cys Gln Val Thr Gly Lys Pro 365  
Thr Pro Thr Val Lys Trp Val Lys Asn Gly Asp Met Val Ile Pro Ser 380  
Asp Tyr Phe Lys Ile Val Lys Gln His Asn Leu Gln Val Leu Gly Leu 400  
Val Lys Ser Asp Gln Gly Phe Tyr Gln Cys Ile Ala Gln Asn Asp Val 415  
Gly Asn Ala Gln Ala Gly Ala Gln Leu Ile Ile Leu Gln His Ala Pro 430  
Ala Thr Thr Gly Pro Leu Pro Ser Ala Pro Arg Asp Val Val Ala Ser 445  
Leu Val Ser Thr Arg Phe Ile Lys Leu Thr Trp Arg Thr Pro Ala Ser 460  
Asp Pro His Gly Asp Asn Leu Thr Tyr Ser Val Phe Tyr Thr Lys Gln 480  
Gly Ile Ala Arg Gln Arg Val Gln Asn Thr Ser His Pro Gly Gln Met 495  
Gln Val Thr Ile Gln Asn Leu Met Pro Ala Thr Val Tyr Ile Phe Arg 510  
Val Met Ala Gln Asn Lys His Gly Ser Gly Gln Ser Ser Ala Pro Leu 525  
Arg Val Gln Thr Gln Pro Gln Val Gln Leu Pro Gly Pro Ala Pro Asn 540  
Leu Arg Ala Tyr Ala Ala Ser Pro Thr Ser Ile Thr Val Thr Trp Gln 560  
Thr Pro Val Ser Gly Asn Gly Gln Ile Gln Asn Tyr Lys Leu Tyr Tyr 575  
Met Gln Lys Gly Thr Asp Lys Gln Gln Asp Val Asp Val Ser Ser His 590  
Ser Tyr Thr Ile Asn Gly Leu Lys Lys Tyr Thr Gln Tyr Ser Phe Arg 605  
Val Val Ala Tyr Asn Lys His Gly Pro Gly Val Ser Thr Pro Asp Val 620  
Ala Val Arg Thr Leu Ser Asp Val Pro Ser Ala Ala Pro Gln Asn Leu 635  
625 630 640

Ser Leu Glu Val Arg Asn Ser Lys Ser Ile Met Ile His Trp Gln Pro 655  
645  
Pro Ala Pro Ala Thr Gln Asn Gly Gln Ile Thr Gly Tyr Lys Ile Arg 670  
660  
Tyr Arg Lys Ala Ser Arg Lys Ser Asp Val Thr Glu Thr Leu Val Ser 685  
675  
Gly Thr Gln Leu Ser Gln Leu Ile Glu Gly Leu Asp Arg Gly Thr Glu 700  
690  
Tyr Asn Phe Arg Val Ala Ala Leu Thr Ile Asn Gly Thr Gly Pro Ala 720  
705  
Thr Asp Trp Leu Ser Ala Glu Thr Phe Glu Ser Asp Leu Asp Glu Thr 735  
725  
Arg Val Pro Glu Val Pro Ser Ser Leu His Val Arg Pro Leu Val Thr 750  
740  
Ser Ile Val Val Ser Trp Thr Pro Glu Asn Gln Asn Ile Val Val 765  
755  
Arg Gly Tyr Ala Ile Gly Tyr Gly Ile Gly Ser Pro His Ala Gln Thr 780  
770  
Ile Lys Val Asp Tyr Lys Gln Arg Tyr Tyr Thr Ile Glu Asn Leu Asp 800  
785  
Pro Ser Ser His Tyr Val Ile Thr Leu Lys Ala Phe Asn Asn Val Gly 815  
805  
Glu Gly Ile Pro Leu Tyr Glu Ser Ala Val Thr Arg Pro His Thr Asp 830  
820  
Thr Ser Glu Val Asp Leu Phe Val Ile Asn Ala Pro Tyr Thr Pro Val 845  
835  
Pro Asp Pro Thr Pro Met Met Pro Pro Val Gly Val Gln Ala Ser Ile 860  
850  
Leu Ser His Asp Thr Ile Arg Ile Thr Trp Ala Asp Asn Ser Leu Pro 880  
865  
Lys His Gln Lys Ile Thr Asp Ser Arg Tyr Tyr Thr Val Arg Trp Lys 895  
885  
Thr Asn Ile Pro Ala Asn Thr Lys Tyr Lys Asn Ala Asn Ala Thr Thr 910  
900  
Leu Ser Tyr Leu Val Thr Gly Leu Lys Pro Asn Thr Leu Tyr Glu Phe 925  
915  
Ser Val Met Val Thr Lys Gly Arg Arg Ser Ser Thr Trp Ser Met Thr 940  
930  
Ala His Gly Thr Thr Phe Glu Leu Val Pro Thr Ser Pro Pro Lys Asp 960  
945

Val Thr Val Val Ser Lys Glu Gly Lys Pro Lys Thr Ile Ile Val Asn 975  
965  
Trp Gln Pro Pro Ser Glu Ala Asn Gly Lys Ile Thr Gly Tyr Ile Ile 990  
985  
Tyr Tyr Ser Thr Asp Val Asn Ala Glu Ile His Asp Trp Val Ile Glu 1005  
995  
Pro Val Val Gly Asn Arg Leu Thr His Gln Ile Gln Glu Leu Thr 1020  
1010  
Leu Asp Thr Pro Tyr Tyr Phe Lys Ile Gln Ala Arg Asn Ser Lys 1035  
1025  
Gly Met Gly Pro Met Ser Glu Ala Val Gln Phe Arg Thr Pro Lys 1050  
1040  
Ala Asp Ser Ser Asp Lys Met Pro Asn Asp Gln Ala Ser Gly Ser 1065  
1055  
Gly Gly Lys Gly Ser Arg Leu Pro Asp Leu Gly Ser Asp Tyr Lys 1080  
1070  
Pro Pro Met Ser Gly Ser Asn Ser Pro His Gly Ser Pro Thr Ser 1095  
1085  
Pro Leu Asp Ser Asn Met Leu Leu Val Ile Ile Val Ser Val Gly 1110  
1100  
Val Ile Thr Ile Val Val Val Val Ile Ile Ala Val Phe Cys Thr 1125  
1115  
Arg Arg Thr Thr Ser His Gln Lys Lys Lys Arg Ala Ala Cys Lys 1140  
1130  
Ser Val Asn Gly Ser His Lys Tyr Lys Gly Asn Ser Lys Asp Val 1155  
1145  
Lys Pro Pro Asp Leu Trp Ile His His Glu Arg Leu Glu Leu Lys 1170  
1160  
Pro Ile Asp Lys Ser Pro Asp Pro Asn Pro Ile Met Thr Asp Thr 1185  
1175  
Pro Ile Pro Arg Asn Ser Gln Asp Ile Thr Pro Val Asp Asn Ser 1200  
1190  
Met Asp Ser Asn Ile His Gln Arg Arg Asn Ser Tyr Arg Gly His 1215  
1205  
Glu Ser Glu Asp Ser Met Thr Leu Ala Gly Arg Gly Met 1230  
1220  
Arg Pro Lys Met Met Met Pro Phe Asp Ser Gln Pro Pro Gln Pro 1245  
1235  
Val Ile Ser Ala His Pro Ile His Ser Leu Asp Asn Pro His His

1250 1255 1260  
His Phe His Ser Ser Ser Leu Ala Ser Pro Ala Arg Ser His Leu  
1265 1270 1275  
Tyr His Pro Gly Ser Pro Trp Pro Ile Gly Thr Ser Met Ser Leu  
1280 1285 1290  
Ser Asp Arg Ala Asn Ser Thr Glu Ser Val Arg Asn Thr Pro Ser  
1295 1300 1305  
Thr Asp Thr Met Pro Ala Ser Ser Ser Gln Thr Cys Cys Thr Asp  
1310 1315 1320  
His Gln Asp Pro Glu Gly Ala Thr Ser Ser Tyr Leu Ala Ser  
1325 1330 1335  
Ser Gln Glu Glu Asp Ser Gly Gln Ser Leu Pro Thr Ala His Val  
1340 1345 1350  
Arg Pro Ser His Pro Leu Lys Ser Phe Ala Val Pro Ala Ile Pro  
1355 1360 1365  
Pro Pro Gly Pro Pro Thr Tyr Asp Pro Ala Leu Pro Ser Thr Pro  
1370 1375 1380  
Leu Leu Ser Gln Gln Ala Leu Asn His His Ile His Ser Val Lys  
1385 1390 1395  
Thr Ala Ser Ile Gly Thr Leu Gly Arg Ser Arg Pro Pro Met Pro  
1400 1405 1410  
Val Val Val Pro Ser Ala Pro Glu Val Gln Glu Thr Thr Arg Met  
1415 1420 1425  
Leu Glu Asp Ser Glu Ser Ser Tyr Glu Pro Asp Glu Leu Thr Lys  
1430 1435 1440  
Glu Met Ala His Leu Glu Gly Leu Met Lys Asp Leu Asn Ala Ile  
1445 1450 1455  
Thr Thr Ala  
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Met Val Val Thr Arg Ser Ala Arg Ala Lys Ala Ser Ile Gln Ala Ala  
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Ser Ala Glu Ser Ser Gly Gln Lys Ser Phe Ala Ala Asn Gly Ile Gln  
20 25 30  
Ala His Pro Glu Ser Ser Thr Gly Ser Asp Ala Arg Thr Thr Asp Glu  
35 40 45  
Ser Gln Thr Thr Gly Lys Gln Ser Leu Ile Pro Arg Thr Pro Lys Ala

50 55 60  
Arg Lys Ser Lys Ser Arg Thr Thr Gly Ser Leu Pro Lys Gly Thr Glu  
65 70 75  
Pro Ser Thr Asp Gly Glu Thr Ser Glu Ala Glu Ser Asn Tyr Ser Val  
80 85 90  
Ser Glu His His Asp Thr Ile Leu Arg Val Thr Arg Arg Arg Gln Ile  
95 100 105 110  
Leu Ile Ala Cys Ser Pro Val Ser Ser Val Arg Lys Lys Pro Lys Val  
115 120 125  
Thr Pro Thr Lys Glu Ser Tyr Thr Glu Glu Ile Val Ser Glu Ala Glu  
130 135 140  
Ser His Val Ser Gly Ile Ser Arg Ile Val Leu Pro Thr Glu Lys Thr  
145 150 155 160  
Thr Gly Ala Arg Arg Ser Lys Ala Lys Ser Leu Thr Asp Pro Ser Gln  
165 170 175  
Glu Ser His Thr Glu Ala Ile Ser Asp Ala Glu Thr Ser Ser Ser Asp  
180 185 190  
Ile Ser Phe Ser Gly Ile Ala Thr Arg Arg Thr Arg Ser Met Gln Arg  
195 200 205  
Lys Leu Lys Ala Gln Thr Glu Lys Lys Asp Ser Lys Ile Val Pro Gly  
210 215 220  
Asn Glu Lys Gln Ile Val Gly Thr Pro Val Asn Ser Glu Asp Ser Asp  
225 230 235  
Thr Arg Gln Thr Ser His Leu Gln Ala Arg Ser Leu Ser Glu Ile Asn  
240 245 250 255  
Lys Pro Asn Phe Tyr Asn Asn Asp Phe Asp Asp Phe Ser His Arg  
260 265 270  
Ser Ser Glu Asn Ile Leu Thr Val His Glu Gln Ala Asn Val Glu Ser  
275 280 285  
Leu Lys Glu Thr Lys Gln Asn Cys Lys Asp Leu Asp Glu Asp Ala Asn  
290 295 300  
Gly Ile Thr Asp Glu Gly Lys Glu Ile Asn Glu Lys Ser Ser Gln Leu  
305 310 315 320  
Lys Asn Leu Ser Glu Leu Gln Asp Thr Ser Leu Gln Gln Leu Val Ser  
325 330 335  
Gln Arg His Ser Thr Pro Gln Asn Lys Asn Ala Val Ser Val His Ser  
340 345 350  
Asn Leu Asn Ser Glu Ala Val Met Lys Ser Leu Thr Gln Thr Phe Ala  
355 360 365

Thr Val Glu Val Gly Arg Trp Asn Asn Asn Lys Lys Ser Pro Ile Lys 370  
375  
Ala Ser Asp Leu Thr Lys Phe Gly Asp Cys Gly Gly Ser Asp Asp Glu 385  
390  
Glu Glu Ser Thr Val Ile Ser Val Ser Glu Asp Met Asn Ser Glu Gly 405  
410  
Asn Val Asp Phe Glu Cys Asp Thr Lys Leu Tyr Thr Ser Ala Pro Asn 420  
425  
Thr Ser Gln Gly Lys Asp Asn Ser Val Leu Leu Val Leu Ser Ser Asp 435  
440  
Glu Ser Gln Gln Ser Glu Asn Ser Glu Asn Glu Glu Asp Thr Leu Cys 450  
455  
Phe Val Glu Asn Ser Gly Gln Arg Glu Ser Leu Ser Gly Asp Thr Gly 465  
470  
Ser Leu Ser Cys Asp Asn Ala Leu Phe Val Ile Asp Thr Thr Pro Gly 485  
490  
Met Ser Ala Asp Lys Asn Phe Tyr Leu Glu Glu Glu Asp Lys Ala Ser 500  
505  
Glu Val Ala Ile Glu Glu Glu Lys Glu Glu Glu Asp Glu Lys Ser 515  
520  
Glu Glu Asp Ser Ser Asp His Asp Glu Asn Glu Asp Glu Phe Ser Asp 530  
535  
Glu Glu Asp Phe Leu Asn Ser Thr Lys Ala Lys Leu Leu Lys Leu Thr 545  
550  
Ser Ser Ser Ile Asp Pro Gly Leu Ser Ile Lys Gln Leu Gly Gly Leu 565  
570  
Tyr Ile Asn Phe Asn Ala Asp Lys Leu Gln Ser Asn Lys Arg Thr Leu 580  
585  
Thr Gln Ile Lys Glu Lys Lys Lys Asn Glu Leu Leu Gln Lys Ala Val 595  
600  
Ile Thr Pro Asp Phe Glu Lys Asn His Cys Val Pro Pro Tyr Ser Glu 610  
615  
Ser Lys Tyr Gln Leu Gln Lys Lys Arg Arg Lys Glu Arg Gln Lys Thr 625  
630  
Ala Gly Asp Gly Trp Phe Gly Met Lys Ala Pro Glu Met Thr Asn Glu 645  
650  
Leu Lys Asn Asp Leu Lys Ala Leu Lys Met Arg Ala Ser Met Asp Pro 660  
665  
Lys Arg Phe Tyr Lys Lys Asn Asp Arg Asp Gly Phe Pro Lys Tyr Phe 675  
680

Gln Ile Gly Thr Ile Val Asp Asn Pro Ala Asp Phe Tyr His Ser Arg 690  
695  
Ile Pro Lys Lys Gln Arg Lys Arg Thr Ile Val Glu Asp Cys Trp Leu 705  
710  
Ile Leu Asn Ser Glu Ile Gln Pro Lys Glu Val Leu Arg Asp His Gly 725  
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25  
Asn Leu Ile Ala Gln His Glu Glu Arg Glu Met Arg Gln Lys Lys Leu 35  
40  
Glu Lys Val Met Glu Glu Gly Leu Lys Asp Glu Glu Lys Arg Leu 50  
55  
Arg Arg Ser Ala His Ala Arg Lys Glu Thr Glu Phe Leu Arg Leu Lys 65  
70  
Arg Thr Arg Leu Gly Leu Glu Asp Phe Glu Ser Leu Lys Val Ile Gly 85  
90  
Arg Gly Ala Phe Gly Glu Val Arg Leu Val Gln Lys Lys Asp Thr Gly 100  
105  
His Val Tyr Ala Met Lys Ile Leu Arg Lys Ala Asp Met Leu Glu Lys 115  
120  
Glu Gln Val Gly His Ile Arg Ala Glu Arg Asp Ile Leu Val Glu Ala 130  
135  
Asp Ser Leu Trp Val Val Lys Met Phe Tyr Ser Phe Gln Asp Lys Leu 145  
150  
Asn Leu Tyr Leu Ile Met Glu Phe Leu Pro Gly Gly Asp Met Met Thr 165  
170  
Leu Leu Met Lys Lys Asp Thr Leu Thr Glu Glu Thr Gln Phe Tyr 180  
185  
Ile Ala Glu Thr Val Leu Ala Ile Asp Ser Ile His Gln Leu Gly Phe 195  
200  
Ile His Arg Asp Ile Lys Pro Asp Asn Leu Leu Leu Ser Lys Gly 210  
215  
His Val Lys Leu Ser Asp Phe Gly Leu Cys Thr Gly Leu Lys Ala 225  
230

His Arg Thr Glu Phe Tyr Arg Asn Leu Asn His Ser Leu Pro Ser Asp  
250 255

Phe Thr Phe Gln Asn Met Asn Ser Lys Arg Lys Ala Glu Thr Trp Lys  
260 265 270

Arg Asn Arg Arg Gln Leu Ala Phe Ser Thr Val Gly Thr Pro Asp Tyr  
275 280 285

Ile Ala pro Glu Val Phe Met Gln Thr Gly Tyr Asn Lys Leu Cys Asp  
290 295 300

Trp Trp Ser Leu Gly Val Ile Met Tyr Glu Met Leu Ile Gly Tyr Pro  
305 310 315 320

Pro Phe Cys Ser Glu Thr Pro Gln Glu Thr Tyr Lys Lys Val Met Asn  
320 325 330 335

Trp Lys Glu Thr Leu Thr Phe Pro Pro Glu Val Pro Ile Ser Glu Lys  
340 345 350

Ala Lys Asp Leu Ile Leu Arg Phe Cys Cys Glu Trp Glu His Arg Ile  
350 355 360 365

Gly Ala Pro Gly Val Glu Glu Ile Lys Ser Asn Ser Phe Glu Gly  
370 375 380

Val Asp Trp Glu Glu His Ile Arg Glu Arg Pro Ala Ala Ile Ser Ile Glu  
385 390 395 400

Ile Lys Ser Ile Asp Asp Thr Ser Asn Phe Asp Glu Phe Pro Glu Ser  
405 410 415

Asp Ile Leu Lys Pro Thr Val Ala Thr Ser Asn His Pro Glu Thr Asp  
420 425 430

Tyr Lys Asn Lys Asp Trp Val Phe Ile Asn Tyr Thr Tyr Lys Arg Phe  
435 440 445

Glu Gly Leu Thr Ala Arg Gly Ala Ile Pro Ser Tyr Met Lys Ala Ala  
450 455 460

Lys  
465

<210> 192  
<211> 73  
<212> PRT  
<213> Homo sapiens  
<400> 192

Met Thr Tyr Phe Pro Leu Gly Arg Tyr Pro Val Val Gly Leu Leu Asp  
1 3 10 15

Gln Met Val Val Leu Ser Thr Phe Ser Ser Leu Lys Asn Leu His Ile  
20 25 30

Val Phe His Ser Gly Cys Thr Ser Leu His Ser His Gln Leu Cys Lys  
35 40 45

Arg Val Pro Phe Ser Pro His Pro Arg Gln His Leu Leu Phe Phe Asp  
50 55 60

Phe Trp Ile Lys Ala Ile Leu Ala Glu  
65 70

<210> 193  
<211> 84  
<212> PRT  
<213> Homo sapiens  
<400> 193

Met Val Cys Phe Arg Leu Phe Pro Val Pro Gly Ser Gly Leu Val Leu  
1 5 10 15

Val Cys Leu Val Leu Gly Ala Val Arg Ser Tyr Ala Leu Glu Leu Asn  
20 25 30

Leu Thr Asp Ser Glu Asn Ala Thr Cys Leu Tyr Ala Lys Trp Gln Met  
35 40 45

Asn Phe Thr Val Arg Tyr Glu Thr Thr Asn Lys Thr Tyr Lys Thr Val  
50 55 60

Thr Ile Ser Asp His Gly Thr Val Thr Tyr Asn Gly Ser Ile Cys Gly  
65 70 75 80

Asp Asp Gln Asn Gly Pro Lys Ile Ala Val Gln Phe Gly Pro Gly Phe  
85 90 95

Ser Trp Ile Ala Asn Phe Thr Lys Ala Ala Ser Thr Tyr Ser Ile Asp  
100 105 110

Ser Val Ser Phe Ser Tyr Asn Thr Gly Asp Asn Thr Thr Phe Pro Asp  
115 120 125

Ala Glu Asp Lys Gly Ile Leu Thr Val Asp Glu Leu Leu Ala Ile Arg  
130 135 140

Ile Pro Leu Asn Asp Leu Phe Arg Cys Asn Ser Leu Ser Thr Leu Glu  
145 150 155 160

Lys Asn Asp Val Val Gln His Tyr Trp Asp Val Leu Val Gln Ala Phe  
165 170 175

Val Gln Asn Gly Thr Val Ser Thr Asn Glu Phe Leu Cys Asp Lys Asp  
180 185 190

Lys Thr Ser Thr Val Ala Pro Thr Ile His Thr Thr Val Pro Ser Pro  
195 200 205

Thr Thr Thr Pro Thr Pro Lys Glu Lys Pro Glu Ala Gly Thr Tyr Ser  
210 215 220

Val Asn Asn Gly Asn Asp Thr Cys Leu Leu Ala Thr Met Gly Leu Gln  
225 230 235 240

Leu Asn Ile Thr Gln Asp Lys Val Ala Ser Val Ile Asn Ile Asn Pro  
245 250 255

Asn Thr Thr His Ser Thr Gly Ser Cys Arg Ser His Thr Ala Leu Leu  
 260 265 270  
 Arg Leu Asn Ser Ser Thr Ile Lys Tyr Leu Asp Phe Val Phe Ala Val  
 275 280 285  
 Lys Asn Glu Asn Arg Phe Tyr Leu Lys Glu Val Asn Ile Ser Met Tyr  
 290 295 300  
 Leu Val Asn Gly Ser Val Phe Ser Ile Ala Asn Asn Asn Leu Ser Tyr  
 305 310 315 320  
 Trp Asp Ala Pro Leu Gly Ser Ser Tyr Met Cys Asn Lys Glu Gln Thr  
 325 330 335  
 Val Ser Val Ser Gly Ala Phe Gln Ile Asn Thr Phe Asp Leu Arg Val  
 340 345 350  
 Gln Pro Phe Asn Val Thr Gln Gly Lys Tyr Ser Thr Ala Gln Glu Cys  
 355 360 365  
 Ser Leu Asp Asp Thr Ile Leu Ile Pro Ile Ile Val Gly Ala Gly  
 370 375 380  
 Leu Ser Gly Leu Ile Ile Val Ile Val Ile Ala Tyr Val Ile Gly Arg  
 385 390 395 400  
 Arg Lys Ser Tyr Ala Gly Tyr Gln Thr Leu  
 405 410  
 <210> 194  
 <211> 480  
 <212> PRT  
 <213> Homo sapiens  
 <400> 194  
 Met Ala Gly Gly Gly Asp Leu Ser Thr Arg Arg Leu Asn Glu Cys  
 1 5 10 15  
 Ile Ser Pro Val Ala Asn Glu Met Asn His Leu Pro Ala His Ser His  
 20 25 30  
 Asp Leu Gln Arg Met Phe Thr Glu Asp Gln Gly Val Asp Asp Arg Leu  
 35 40 45  
 Leu Tyr Asp Ile Val Phe Lys His Phe Lys Arg Asn Lys Val Glu Ile  
 50 55 60  
 Ser Asn Ala Ile Lys Lys Thr Phe Pro Phe Leu Glu Gly Leu Arg Asp  
 65 70 75 80  
 Arg Asp Leu Ile Thr Asn Lys Met Phe Glu Asp Ser Gln Asp Ser Cys  
 85 90 95  
 Arg Asn Leu Val Pro Val Gln Arg Val Val Tyr Asn Val Leu Ser Glu  
 100 105 110  
 Leu Glu Lys Thr Phe Asn Leu Pro Val Leu Glu Ala Leu Phe Ser Asp  
 115 120 125

Val Asn Met Gln Glu Tyr Pro Asp Leu Ile His Ile Tyr Lys Gly Phe  
 130 135 140  
 Glu Asn Val Ile His Asp Lys Leu Pro Leu Gln Glu Ser Glu Glu Glu  
 145 150 155 160  
 Glu Arg Glu Glu Arg Ser Gly Leu Gln Leu Ser Leu Glu Gln Gly Thr  
 165 170 175  
 Gly Glu Asn Ser Phe Arg Ser Leu Thr Trp Pro Pro Ser Gly Ser Pro  
 180 185 190  
 Ser His Ala Gly Thr Thr Pro Glu Asn Gly Leu Ser Glu His Pro  
 195 200 205  
 Cys Glu Thr Glu Gln Ile Asn Ala Lys Arg Lys Asp Thr Thr Ser Asp  
 210 215 220  
 Lys Asp Asp Ser Leu Gly Ser Gln Gln Thr Asn Glu Gln Cys Ala Gln  
 225 230 235 240  
 Lys Ala Glu Pro Thr Glu Ser Cys Glu Gln Ile Ala Val Gln Val Asn  
 245 250 255  
 Asn Gly Asp Ala Gly Arg Glu Met Pro Cys Pro Leu Pro Cys Asp Glu  
 260 265 270  
 Glu Ser Pro Glu Ala Glu Leu His Asn His Gly Ile Gln Ile Asn Ser  
 275 280 285  
 Cys Ser Val Arg Leu Val Asp Ile Lys Lys Glu Lys Pro Phe Ser Asn  
 290 295 300  
 Ser Lys Val Glu Cys Gln Ala Gln Ala Arg Thr His His Asn Gln Ala  
 305 310 315 320  
 Ser Asp Ile Ile Val Ile Ser Ser Glu Asp Ser Glu Gly Ser Thr Asp  
 325 330 335  
 Val Asp Glu Pro Leu Glu Val Phe Ile Ser Ala Pro Arg Ser Glu Pro  
 340 345 350  
 Val Ile Asn Asn Asp Asn Pro Leu Glu Ser Asn Asp Glu Lys Glu Gly  
 355 360 365  
 Gln Glu Ala Thr Cys Ser Arg Pro Gln Ile Val Pro Glu Pro Met Asp  
 370 375 380  
 Phe Arg Lys Leu Ser Thr Phe Arg Glu Ser Phe Lys Lys Arg Val Ile  
 385 390 395 400  
 Gly Gln Asp His Asp Phe Ser Glu Ser Ser Glu Glu Glu Ala Pro Ala  
 405 410 415  
 Glu Ala Ser Ser Gly Ala Leu Arg Ser Lys His Gly Glu Lys Ala Pro  
 420 425 430  
 Met Thr Ser Arg Ser Thr Ser Thr Trp Arg Ile Pro Ser Arg Lys Arg  
 435 440 445



Arg Phe Ser Ser Ser Asp Phe Ser Asp Leu Ser Asn Gly Glu Glu Leu  
430 435 460

Gln Glu Thr Cys Ser Ser Ser Leu Arg Arg Gly Ser Gly Lys Glu Asp  
465 470 475

<210> 195  
<211> 339  
<212> PRT  
<213> Homo sapiens  
<400> 195

Met Trp Gln Leu Trp Ala Ser Leu Cys Cys Leu Leu Val Leu Ala Asn  
1 5 10 15

Ala Arg Ser Arg Pro Ser Phe His Pro Leu Ser Asp Glu Leu Val Asn  
20 25 30

Tyr Val Asn Lys Arg Asn Thr Thr Trp Gln Ala Gly His Asn Phe Tyr  
35 40 45

Asn Val Asp Met Ser Tyr Leu Lys Arg Leu Cys Gly Thr Phe Leu Gly  
50 55 60

Gly Pro Lys Pro Pro Gln Arg Val Met Phe Thr Glu Asp Leu Lys Leu  
65 70 75 80

Pro Ala Ser Phe Asp Ala Arg Glu Gln Trp Pro Gln Cys Pro Thr Ile  
85 90 95

Lys Glu Ile Arg Asp Gln Gly Ser Cys Gly Ser Cys Trp Ala Phe Gly  
100 105 110

Ala Val Glu Ala Ile Ser Asp Arg Ile Cys Ile His Thr Asn Ala His  
115 120 125

Val Ser Val Glu Val Ser Ala Glu Asp Leu Leu Thr Cys Cys Gly Ser  
130 135 140

Met Cys Gly Asp Gly Cys Asn Gly Gly Tyr Pro Ala Glu Ala Trp Asn  
145 150 155 160

Phe Trp Thr Arg Lys Gly Leu Val Ser Gly Gly Leu Tyr Glu Ser His  
165 170 175

Val Gly Cys Arg Pro Tyr Ser Ile Pro Pro Cys Glu His His Val Asn  
180 185 190

Gly Ser Arg Pro Pro Cys Thr Gly Glu Gly Asp Thr Pro Lys Cys Ser  
195 200 205

Lys Ile Cys Glu Pro Gly Tyr Ser Pro Thr Tyr Lys Gln Asp Lys His  
210 215 220

Tyr Gly Tyr Asn Ser Tyr Ser Val Ser Asn Ser Glu Lys Asp Ile Met  
225 230 235

Ala Glu Ile Tyr Lys Asn Gly Pro Val Glu Gly Ala Phe Ser Val Tyr  
240 245 250 255

Ser Asp Phe Leu Leu Tyr Lys Ser Gly Val Tyr Gln His Val Thr Gly  
260 265 270

Glu Met Met Gly Gly His Ala Ile Arg Ile Leu Gly Trp Gly Val Glu  
275 280 285

Asn Gly Thr Pro Tyr Trp Leu Val Ala Asn Ser Trp Asn Thr Asp Trp  
290 295 300

Gly Asp Asn Gly Phe Phe Lys Ile Leu Arg Gly Gln Asp His Cys Gly  
305 310 315 320

Ile Glu Ser Glu Val Val Ala Gly Ile Pro Arg Thr Asp Gln Tyr Trp  
325 330 335

Glu Lys Ile

<210> 196  
<211> 2328  
<212> PRT  
<213> Homo sapiens  
<400> 196

Lys Ser Lys Arg Gln Ala Gln Gln Met Val Gln Pro Gln Ser Pro Val  
1 5 10 15

Ala Val Ser Gln Ser Lys Pro Gly Cys Tyr Asp Asn Gly Lys His Tyr  
20 25 30

Gln Ile Asn Gln Gln Trp Glu Arg Thr Tyr Leu Gly Asn Val Leu Val  
35 40 45

Cys Thr Cys Tyr Gly Gly Ser Arg Gly Phe Asn Cys Glu Ser Lys Pro  
50 55 60

Glu Ala Glu Glu Thr Cys Phe Asp Lys Tyr Thr Gly Asn Thr Tyr Arg  
65 70 75 80

Val Gly Asp Thr Tyr Glu Arg Pro Lys Asp Ser Met Ile Trp Asp Cys  
85 90 95

Thr Cys Ile Gly Ala Gly Arg Gly Arg Ile Ser Cys Thr Ile Ala Asn  
100 105 110

Arg Cys His Glu Gly Gly Gln Ser Tyr Lys Ile Gly Asp Thr Trp Arg  
115 120 125

Arg Pro His Glu Thr Gly Tyr Met Leu Glu Cys Val Cys Leu Gly  
130 135 140

Asn Gly Lys Gly Glu Trp Thr Cys Lys Pro Ile Ala Glu Lys Cys Phe  
145 150 155 160

Asp His Ala Ala Gly Thr Ser Tyr Val Val Gly Glu Thr Trp Glu Lys  
165 170 175

Pro Tyr Gln Gly Trp Met Met Val Asp Cys Thr Cys Leu Gly Glu Gly  
180 185 190

Ser Gly Arg Ile Thr Cys Thr Ser Arg Asn Arg Cys Asn Asp Gln Asp 205  
195  
Thr Arg Thr Ser Tyr Arg Ile Gly Asp Thr Trp Ser Lys Lys Asp Asn 220  
210  
Arg Gly Asn Leu Leu Gln Cys Ile Cys Thr Gly Asn Gly Arg Gly Glu 225  
230  
Trp Lys Cys Glu Arg His Thr Ser Val Gln Thr Thr Ser Ser Gly Ser 245  
250  
Gly Pro Phe Thr Asp Val Arg Ala Val Tyr Gln Pro Gln Pro His 260  
265  
Pro Gln Pro Pro Tyr Gly His Cys Val Thr Asp Ser Gly Val Val 275  
280  
Tyr Ser Val Gly Met Gln Trp Leu Lys Thr Gln Gly Asn Lys Gln Met 285  
290  
Leu Cys Thr Cys Leu Gly Asn Gly Val Ser Cys Gln Glu Thr Ala Val 305  
310  
Thr Gln Thr Tyr Gly Gly Asn Leu Asn Gly Glu Pro Cys Val Leu Pro 325  
330  
Phe Thr Tyr Asn Gly Arg Thr Phe Tyr Ser Cys Thr Thr Glu Gly Arg 340  
345  
Gln Asp Gly His Leu Trp Cys Ser Thr Thr Ser Asn Tyr Glu Gln Asp 350  
355  
Gln Lys Tyr Ser Phe Cys Thr Asp His Thr Val Leu Val Gln Thr Gln 370  
375  
Gly Gly Asn Ser Asn Gly Ala Leu Cys His Phe Pro Phe Leu Tyr Asn 385  
390  
Asn His Asn Tyr Thr Asp Cys Thr Ser Glu Gly Arg Asp Asn Met 405  
410  
Lys Trp Cys Gly Thr Thr Gln Asn Tyr Asp Ala Asp Gln Lys Phe Gly 420  
425  
Phe Cys Pro Met Ala Ala His Glu Glu Ile Cys Thr Thr Asn Glu Gly 435  
440  
Val Met Tyr Arg Ile Gly Asp Gln Trp Asp Lys Gln His Asp Met Gly 450  
455  
His Met Met Arg Cys Thr Cys Val Gly Asn Gly Arg Gly Glu Trp Thr 465  
470  
Cys Ile Ala Tyr Ser Gln Leu Arg Asp Gln Cys Ile Val Asp Asp Ile 485  
490  
Thr Tyr Asn Val Asn Asp Thr Phe His Lys Arg His Glu Glu Gly His

300 505 510  
Met Leu Asn Cys Thr Cys Phe Gly Gln Gly Arg Gly Arg Trp Lys Cys 515  
520  
Asp Pro Val Asp Gln Cys Gln Asp Ser Glu Thr Gly Thr Phe Tyr Gln 530  
535  
Ile Gly Asp Ser Trp Glu Lys Tyr Val His Gly Val Arg Tyr Gln Cys 545  
550  
Tyr Cys Tyr Gly Arg Gly Ile Gly Glu Trp His Cys Gln Pro Leu Gln 565  
570  
Thr Tyr Pro Ser Ser Gly Pro Val Glu Val Phe Ile Thr Glu Thr 580  
585  
Pro Ser Gln Pro Asn Ser His Pro Ile Gln Trp Asn Ala Pro Gln Pro 595  
600  
Ser His Ile Ser Lys Tyr Ile Leu Arg Trp Arg Pro Lys Asn Ser Val 610  
615  
Gly Arg Trp Lys Glu Ala Thr Ile Pro Gly His Leu Asn Ser Tyr Thr 625  
630  
Ile Lys Gly Leu Lys Pro Gly Val Val Tyr Glu Gly Gln Leu Ile Ser 645  
650  
Ile Gln Gln Tyr Gly His Gln Glu Val Thr Arg Phe Asp Phe Thr Thr 660  
665  
Thr Ser Thr Ser Thr Pro Val Thr Ser Asn Thr Val Thr Gly Glu Thr 675  
680  
Thr Pro Phe Ser Pro Leu Val Ala Thr Ser Glu Ser Val Thr Glu Ile 690  
695  
Thr Ala Ser Ser Phe Val Val Ser Trp Val Ser Ala Ser Asp Thr Val 705  
710  
Ser Gly Phe Arg Val Glu Tyr Glu Leu Ser Glu Glu Gly Asp Glu Pro 725  
730  
Gln Tyr Leu Asp Leu Pro Ser Thr Ala Thr Ser Val Asn Ile Pro Asp 740  
745  
Leu Leu Pro Gly Arg Lys Tyr Ile Val Asn Val Tyr Gln Ile Ser Glu 755  
760  
Asp Gly Glu Gln Ser Leu Ile Leu Ser Thr Ser Gln Thr Thr Ala Pro 770  
775  
Asp Ala Pro Pro Asp Pro Thr Val Asp Gln Val Asp Asp Thr Ser Ile 785  
790  
Val Val Arg Trp Ser Arg Pro Gln Ala Pro Ile Thr Gly Tyr Arg Ile 805  
810

Val Tyr Ser Pro Ser Val Glu Gly Ser Ser Thr Glu Leu Asn Leu Pro  
820 825 830  
Glu Thr Ala Asn Ser Val Thr Leu Ser Asp Leu Gln Pro Gly Val Gln  
835 840 845  
Tyr Asn Ile Thr Ile Tyr Ala Val Glu Asn Gln Glu Ser Thr Pro  
850 855 860  
Val Val Ile Gln Gln Glu Thr Thr Gly Thr Pro Arg Ser Asp Thr Val  
865 870 875 880  
Pro Ser Pro Arg Asp Leu Gln Phe Val Glu Val Thr Asp Val Lys Val  
885 890 895  
Thr Ile Met Trp Thr Pro Pro Glu Ser Ala Val Thr Gly Tyr Arg Val  
900 905 910  
Asp Val Ile Pro Val Asn Leu Pro Glu Gly Glu His Gly Gln Arg Leu Pro  
915 920 925  
Ile Ser Arg Asn Thr Phe Ala Glu Val Thr Gly Leu Ser Pro Gly Val  
930 935 940  
Thr Tyr Tyr Phe Lys Val Phe Ala Val Ser His Gly Arg Glu Ser Lys  
945 950 955  
Pro Leu Thr Ala Gln Gln Thr Thr Lys Leu Asp Ala Pro Thr Asn Leu  
965 970 975  
Gln Phe Val Asn Glu Thr Asp Ser Thr Val Leu Val Arg Trp Thr Pro  
980 985 990  
Pro Arg Ala Gln Ile Thr Gly Tyr Arg Leu Thr Val Gly Leu Thr Arg  
995 1000 1005  
Arg Gly Gln Pro Arg Gln Tyr Asn Val Gly Pro Ser Val Ser Lys  
1010 1015 1020  
Tyr Pro Leu Arg Asn Leu Gln Pro Ala Ser Glu Tyr Thr Val Ser  
1025 1030 1035  
Leu Val Ala Ile Lys Gly Asn Gln Glu Ser Pro Lys Ala Thr Gly  
1040 1045 1050  
Val Phe Thr Thr Leu Gln Thr Pro Gly Ser Ser Ile Pro Pro Tyr Asn  
1055 1060 1065  
Thr Glu Val Thr Glu Thr Thr Ile Val Ile Thr Trp Thr Pro Ala  
1070 1075 1080  
Pro Arg Ile Gly Phe Lys Leu Gly Val Arg Pro Ser Gln Gly Gly  
1085 1090 1095  
Glu Ala Pro Arg Gln Val Thr Ser Asp Ser Gly Ser Ile Val Val  
1100 1105 1110  
Ser Gly Leu Thr Pro Gly Val Glu Tyr Val Tyr Thr Ile Gln Val  
1115 1120 1125

Leu Arg Asp Gly Gln Glu Arg Asp Ala Pro Ile Val Asn Lys Val  
1130 1135 1140  
Val Thr Pro Leu Ser Pro Pro Thr Asn Leu His Leu Glu Ala Asn  
1145 1150 1155  
Pro Asp Thr Gly Val Leu Thr Val Ser Trp Glu Arg Ser Thr Thr  
1160 1165 1170  
Pro Asp Ile Thr Gly Tyr Arg Ile Thr Thr Thr Pro Thr Asn Gly  
1175 1180 1185  
Gln Gln Gly Asn Ser Leu Glu Glu Val Val His Ala Asp Gln Ser  
1190 1195 1200  
Ser Cys Thr Phe Asp Asn Leu Ser Pro Gly Leu Glu Tyr Asn Val  
1205 1210 1215  
Ser Val Tyr Thr Val Lys Asp Asp Lys Glu Ser Val Pro Ile Ser  
1220 1225 1230  
Asp Thr Ile Ile Pro Ala Val Pro Pro Pro Thr Asp Leu Arg Phe  
1235 1240 1245  
Thr Asn Ile Gly Pro Asp Thr Met Arg Val Thr Trp Ala Pro Pro  
1250 1255 1260  
Pro Ser Ile Asp Leu Thr Asn Phe Leu Val Arg Tyr Ser Pro Val  
1265 1270 1275  
Lys Asn Glu Glu Asp Val Ala Glu Leu Ser Ile Ser Pro Ser Asp  
1280 1285 1290  
Asn Ala Val Val Leu Thr Asn Leu Leu Pro Gly Thr Glu Tyr Val  
1295 1300 1305  
Val Ser Val Ser Ser Val Tyr Glu Gln His Glu Ser Thr Pro Leu  
1310 1315 1320  
Arg Gly Arg Gln Lys Thr Gly Leu Asp Ser Pro Thr Gly Ile Asp  
1325 1330 1335  
Phe Ser Asp Ile Thr Ala Asn Ser Phe Thr Val His Trp Ile Ala  
1340 1345 1350  
Pro Arg Ala Thr Ile Thr Gly Tyr Arg Ile Arg His His Pro Glu  
1355 1360 1365  
His Phe Ser Gly Arg Pro Arg Glu Asp Arg Val Pro His Ser Arg  
1370 1375 1380  
Asn Ser Ile Thr Leu Thr Asn Leu Thr Pro Gly Thr Glu Tyr Val  
1385 1390 1395  
Val Ser Ile Val Ala Leu Asn Gly Arg Glu Glu Ser Pro Leu Leu  
1400 1405 1410  
Ile Gly Gln Gln Ser Thr Val Ser Asp Val Pro Arg Asp Leu Glu  
1415 1420 1425

Val Val Ala Ala Thr Pro Thr Ser Leu Leu Ile Ser Trp Asp Ala  
1430 1435 1440

Pro Ala Val Thr Val Arg Tyr Tyr Arg Ile Thr Tyr Gly Glu Thr  
1445 1450 1455

Gly Gly Asn Ser Pro Val Gln Glu Phe Thr Val Pro Gly Ser Lys  
1460 1465 1470

Ser Thr Ala Thr Ile Ser Gly Leu Lys Pro Gly Val Asp Tyr Thr  
1475 1480 1485

Ile Thr Val Tyr Ala Val Thr Gly Arg Gly Asp Ser Pro Ala Ser  
1490 1495 1500

Ser Lys Pro Ile Ser Ile Asn Tyr Arg Thr Glu Ile Asp Lys Pro  
1505 1510 1515

Ser Gln Met Gln Val Thr Asp Val Gln Asn Ser Ile Ser Val  
1520 1525 1530

Lys Trp Leu Pro Ser Ser Ser Pro Val Thr Gly Tyr Arg Val Thr  
1535 1540 1545

Thr Thr Pro Lys Asn Gly Pro Gly Pro Thr Lys Thr Lys Thr Ala  
1550 1555 1560

Gly Pro Asp Gln Thr Glu Met Thr Ile Glu Gly Leu Gln Pro Thr  
1565 1570 1575

Val Glu Tyr Val Val Ser Val Tyr Ala Gln Asn Pro Ser Gly Glu  
1580 1585 1590

Ser Gln Pro Leu Val Gln Thr Ala Val Thr Asn Ile Asp Arg Pro  
1595 1600 1605

Lys Gly Leu Ala Phe Thr Asp Val Asp Val Asp Ser Ile Lys Ile  
1610 1615 1620

Ala Trp Glu Ser Pro Gln Gly Gln Val Ser Arg Tyr Arg Val Thr  
1625 1630 1635

Tyr Ser Ser Pro Glu Asp Gly Ile His Glu Leu Phe Pro Ala Pro  
1640 1645 1650

Asp Gly Glu Asp Thr Ala Glu Leu Gln Gly Leu Arg Pro Gly  
1655 1660 1665

Ser Glu Tyr Thr Val Ser Val Val Ala Leu His Asp Asp Met Glu  
1670 1675 1680

Ser Gln Pro Leu Ile Gly Thr Gln Ser Thr Ala Ile Pro Ala Pro  
1685 1690 1695

Thr Asp Leu Lys Phe Thr Gln Val Thr Pro Thr Ser Leu Ser Ala  
1700 1705 1710

Gln Trp Thr Pro Pro Asn Val Gln Leu Thr Gly Tyr Arg Val Arg

1715 1720 1725

Val Thr Pro Lys Glu Lys Thr Gly Pro Met Lys Glu Ile Asn Leu  
1730 1735 1740

Ala Pro Asp Ser Ser Ser Val Val Val Ser Gly Leu Met Val Ala  
1745 1750 1755

Thr Lys Tyr Glu Val Ser Val Tyr Ala Leu Lys Asp Thr Leu Thr  
1760 1765 1770

Ser Arg Pro Ala Gln Gly Val Val Thr Thr Leu Glu Asn Val Ser  
1775 1780 1785

Pro Pro Arg Arg Ala Arg Val Thr Asp Ala Thr Glu Thr Thr Ile  
1790 1795 1800

Thr Ile Ser Trp Arg Thr Lys Thr Glu Thr Thr Thr Gly Phe Gln  
1805 1810 1815

Val Asp Ala Val Pro Ala Asn Gly Gln Thr Thr Pro Ile Gln Arg Thr  
1820 1825 1830

Ile Lys Pro Asp Val Arg Ser Tyr Thr Thr Thr Gly Leu Gln Pro  
1835 1840 1845

Gly Thr Asp Tyr Lys Ile Tyr Leu Tyr Thr Leu Asn Asp Asn Ala  
1850 1855 1860

Arg Ser Ser Pro Val Val Ile Asp Ala Ser Thr Ala Ile Asp Ala  
1865 1870 1875

Pro Ser Asn Leu Arg Phe Leu Ala Thr Thr Thr Pro Asn Ser Leu Leu  
1880 1885 1890

Val Ser Trp Gln Pro Pro Arg Ala Arg Ile Thr Gly Tyr Ile Ile  
1895 1900 1905

Lys Tyr Glu Lys Pro Gly Ser Pro Pro Arg Glu Val Val Pro Arg  
1910 1915 1920

Pro Arg Pro Gly Val Thr Glu Ala Thr Thr Thr Gly Leu Glu Pro  
1925 1930 1935

Gly Thr Glu Tyr Thr Thr Tyr Val Ile Ala Leu Lys Asn Asn Gln  
1940 1945 1950

Lys Ser Glu Pro Leu Ile Gly Arg Lys Lys Thr Asp Glu Leu Pro  
1955 1960 1965

Gln Leu Val Thr Leu Pro His Pro Asn Leu His Gly Pro Glu Ile  
1970 1975 1980

Leu Asp Val Pro Ser Thr Val Gln Lys Thr Thr Phe Val Thr His  
1985 1990 1995

Pro Gly Tyr Asp Thr Gly Asn Gly Ile Gln Leu Pro Gly Thr Ser  
2000 2005 2010

Gly Gln Gln Pro Ser Val Gly Gln Gln Met Ile Phe Glu Glu His  
2015 2030 2025

Gly Phe Arg Arg Thr Thr Pro Pro Thr Thr Ala Thr Pro Ile Arg  
2030 2035 2040

His Arg Pro Arg Pro Tyr Pro Pro Asn Val Gly Gln Glu Ala Leu  
2045 2050 2055

Ser Gln Thr Thr Ile Ser Thr Ala Pro Phe Gln Asp Thr Ser Glu  
2060 2065 2070

Tyr Ile Ile Ser Cys His Pro Val Gly Thr Asp Glu Glu Pro Leu  
2075 2080 2085

Gln Phe Arg Val Pro Gly Thr Ser Thr Ser Ala Thr Leu Thr Gly  
2090 2095 2100

Leu Thr Arg Gly Ala Thr Tyr Asn Ile Ile Val Glu Ala Leu Lys  
2105 2110 2115

Asp Gln Gln Arg His Lys Val Arg Glu Glu Val Val Thr Val Gly  
2120 2125 2130

Asn Ser Val Asn Glu Gly Leu Asn Gln Pro Thr Asp Asp Ser Cys  
2135 2140 2145

Phe Asp Pro Tyr Thr Val Ser His Tyr Ala Val Gly Asp Glu Thr  
2150 2155 2160

Glu Arg Met Ser Glu Ser Gly Phe Lys Leu Leu Cys Gln Cys Leu  
2165 2170 2175

Gly Phe Gly Ser Gly His Phe Arg Cys Asp Ser Ser Arg Thr Cys  
2180 2185 2190

His Asp Asn Gly Val Asn Tyr Lys Ile Gly Glu Lys Thr Asp Arg  
2195 2200 2205

Gln Gly Glu Asn Gly Gln Met Met Ser Cys Thr Cys Leu Gly Asn  
2210 2215 2220

Gly Lys Gly Glu Phe Lys Cys Asp Pro His Glu Ala Thr Cys Tyr  
2225 2230 2235

Asp Asp Gly Lys Thr Tyr His Val Gly Glu Gln Thr Gln Lys Glu  
2240 2245 2250

Tyr Leu Gly Ala Ile Cys Ser Cys Thr Cys Phe Gly Gly Gln Arg  
2255 2260 2265

Gly Thr Arg Cys Asp Asn Cys Arg Arg Pro Gly Gly Glu Pro Ser  
2270 2275 2280

Pro Glu Gly Thr Thr Gly Gln Ser Tyr Asn Gln Tyr Ser Gln Arg  
2285 2290 2295

Tyr His Gln Arg Thr Asn Thr Asn Val Asn Cys Pro Ile Glu Cys  
2300 2305 2310

Phe Met Pro Leu Asp Val Gln Ala Asp Arg Glu Asp Ser Arg Glu  
2315 2320 2325

<210> 197  
<211> 165  
<212> PRT  
<213> Homo sapiens  
<400> 197

Met Leu Met Pro Lys Lys Asn Arg Ile Ala Ile Tyr Glu Leu Leu Phe  
1 5 10 15

Lys Glu Gly Val Met Val Ala Lys Lys Asp Val His Met Pro Lys His  
20 25 30

Pro Glu Leu Ala Asp Lys Asn Val Pro Asn Leu His Val Met Lys Ala  
35 40 45

Met Gln Ser Leu Lys Ser Arg Gly Tyr Val Lys Glu Gln Phe Ala Thr  
50 55 60

Arg His Phe Tyr Thr Tyr Leu Thr Asn Glu Gly Ile Gln Tyr Leu Arg  
65 70 75 80

Asp Tyr Leu His Leu Pro Glu Ile Val Pro Ala Thr Leu Arg Arg  
85 90 95

Ser Arg Pro Glu Thr Gly Arg Pro Arg Pro Lys Gly Leu Glu Gly Glu  
100 105 110

Arg Pro Ala Arg Leu Thr Arg Gly Glu Ala Asp Arg Asp Thr Tyr Arg  
115 120 125

Arg Ser Ala Val Pro Pro Gly Ala Asp Lys Lys Ala Glu Ala Gly Ala  
130 135 140

Gly Ser Ala Thr Glu Phe Gln Phe Arg Gly Gly Phe Gly Arg Gly Arg  
145 150 155 160

Gly Gln Pro Pro Gln  
165

<210> 198  
<211> 154  
<212> PRT  
<213> Homo sapiens  
<400> 198

Met Ala Thr Lys Ala Val Cys Val Leu Lys Gly Asp Gly Pro Val Gln  
1 5 10 15

Gly Ile Ile Asn Phe Glu Gln Lys Glu Ser Asn Gly Pro Val Lys Val  
20 25 30

Thr Gly Ser Ile Lys Gly Leu Thr Glu Gly Leu His Gly Phe His Val  
35 40 45

His Glu Phe Gly Asp Asn Thr Ala Gly Cys Thr Ser Ala Gly Pro His  
50 55 60

Phe Asn Pro Leu Ser Arg Lys His Gly Gln Pro Lys Asp Glu Arg 80  
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His Val Gly Asp Leu Gly Asn Val Thr Ala Asp Lys Asp Gly Val Ala 95  
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Ile Ile Gly Arg Thr Leu Val Val His Glu Lys Ala Asp Asp Leu Gly 125  
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305 310 315 320  
Arg Asp Val Glu Ser Val Gln Thr Pro Ser Lys Ala Val Gly Ala Ser 335  
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Phe Pro Leu Tyr Glu Pro Ala Lys Met Lys Thr Pro Val Gln Tyr Ser 350  
340 345 350  
Gln Gln Gln Asn Ser Pro Gln Lys His Lys Asn Lys Asp Leu Tyr Thr 365  
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Thr Gly Arg Arg Glu Ser Val Asn Leu Glu Lys Ser Glu Gly Phe Lys 380  
370 375 380  
Ala Gly Asp Lys Thr Leu Thr Pro Arg Lys Leu Ser Thr Arg Asn Arg 400  
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Asn Leu Ser Ser Lys Thr Arg Gly Ser Ile Pro Thr Asp Val Glu Val 430  
420 425 430  
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450 455 460  
Glu Lys Leu Gly Thr Thr Ala Gly Gln Met Cys Ser Gly Leu Pro Gly 480  
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565 570 575  
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Ser Gln Thr Glu Val Pro Lys Arg Gly Glu Arg Val Ala Thr Cys  
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Gln Thr Lys Val Ile Lys His Gly Pro Gln Arg Ser Met Asn Lys Arg  
675 680 685  
Gln Arg Arg Pro-Ala Thr Pro Lys Lys Pro Val Gly Glu Val His Ser  
690 695 700  
Gln Phe Ser Thr Gly His Ala Asn Ser Pro Cys Thr Ile Ile Ile Gly  
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Lys Ala His Thr Glu Lys Val His Val Pro Ala Arg Pro Tyr Arg Val  
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740 745 750  
Ser Gly Ile Ala Glu Met Phe Lys Thr Pro Val Lys Glu Gln Pro Gln  
755 760 765  
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770 775 780  
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785 790 795  
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Ala Lys Gln Pro Ser Asp Lys Cys Ser Ala Ser Pro Pro Leu Arg Arg  
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Tyr Lys Met Thr Ser Leu Glu Thr Lys Thr Ser Asp Thr Glu Thr Glu  
850 855 860  
Pro Ser Lys Thr Val Ser Thr Val Asn Arg Ser Gly Arg Ser Thr Glu  
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Phe Arg Asn Ile Gln Lys Leu Pro Val Glu Ser Lys Ser Glu Glu Thr  
885 890 895  
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980 985 990  
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995 1000 1005  
Ser Leu Gln Pro Glu Pro Ile Asn Thr Pro Thr His Thr Lys Gln  
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Gly Met Lys Lys Trp Pro Arg Thr Pro Lys Glu Glu Ala Gln Ser  
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Cys Lys Ser Pro Pro Pro Glu Ser Val Asp Thr Thr Ser Thr

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Lys Gln Thr Pro Lys Arg Ser Leu Arg Lys Ala Asp Val Glu Glu 1145 1155  
Glu Phe Leu Leu Arg Lys Leu Thr Pro Ser Ala Gly Lys Ala 1160 1170  
Met Leu Thr Pro Lys Pro Ala Gly Gly Asp Glu Lys Asp Ile Lys 1175 1185  
Ala Phe Met Gly Thr Pro Val Gln Lys Leu Asp Leu Ala Gly Thr 1190 1200  
Leu Pro Gly Ser Lys Arg Gln Leu Gln Thr Pro Lys Glu Lys Ala 1205 1215  
Gln Ala Leu Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr 1220 1230  
Pro Gly His Thr Glu Glu Leu Val Ala Ala Gly Lys Thr Thr Lys 1235 1245  
Ile Pro Cys Asp Ser Pro Gln Ser Asp Pro Val Asp Thr Pro Thr 1250 1260  
Ser Thr Lys Gln Arg Pro Lys Arg Ser Ile Arg Lys Ala Asp Val 1265 1275  
Glu Gly Glu Leu Leu Ala Cys Arg Asn Leu Met Pro Ser Ala Gly 1280 1290  
Lys Ala Met His Thr Pro Lys Pro Ser Val Gly Glu Lys Asp 1295 1305  
Ile Ile Ile Phe Val Gly Thr Pro Val Gln Lys Leu Asp Leu Thr 1310 1320  
Glu Asn Leu Thr Gly Ser Lys Arg Arg Pro Gln Thr Pro Lys Glu 1325 1335  
Glu Ala Gln Ala Leu Glu Asp Leu Thr Gly Phe Lys Glu Leu Phe 1340 1350  
Gln Thr Pro Gly His Thr Glu Glu Ala Val Ala Gly Lys Thr 1355 1365  
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Pro Thr Ser Thr Arg Arg Gln Pro Lys Thr Pro Leu Glu Lys Arg 1385 1395  
Asp Val Gln Lys Glu Leu Ser Ala Leu Lys Lys Leu Thr Gln Thr 1400 1410  
Ser Gly Glu Thr Thr His Thr Asp Lys Val Pro Gly Gly Glu Asp 1415 1425

Lys Ser Ile Asn Ala Phe Arg Glu Thr Ala Lys Val Lys Leu Asp 1430 1440  
Pro Ala Ala Ser Val Thr Gly Ser Lys Arg His Pro Lys Thr Lys 1445 1455  
Glu Lys Ala Gln Pro Leu Glu Asp Leu Ala Gly Trp Lys Glu Leu 1460 1470  
Phe Gln Thr Pro Val Cys Thr Asp Lys Pro Thr Thr His Glu Lys 1475 1485  
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Pro Thr Ser Ser Lys Pro Gln Ser Lys Arg Ser Leu Arg Lys Val 1505 1515  
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Ala Gly Lys Ala Met His Thr Pro Lys Pro Ala Val Ser Gly Glu 1535 1545  
Lys Asn Ile Tyr Ala Phe Met Gly Thr Pro Val Gln Lys Leu Asp 1550 1560  
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Lys Glu Lys Ala Gln Ala Leu Glu Asp Leu Ala Gly Phe Lys Glu 1580 1590  
Leu Phe Gln Thr Arg Gly His Thr Glu Glu Ser Met Thr Asn Asp 1595 1605  
Lys Thr Ala Lys Val Ala Cys Lys Ser Ser Gln Pro Asp Leu Asp 1610 1620  
Lys Asn Pro Ala Ser Ser Lys Arg Arg Leu Lys Thr Ser Leu Gly 1625 1635  
Lys Val Gly Val Lys Glu Glu Leu Leu Ala Val Lys Lys Leu Thr 1640 1650  
Gln Thr Ser Gly Glu Thr Thr His Thr His Thr Glu Pro Thr Gly 1655 1665  
Asp Gly Lys Ser Met Lys Ala Phe Met Glu Ser Pro Lys Gln Ile 1670 1680  
Leu Asp Ser Ala Ala Ser Leu Thr Gly Ser Lys Arg Gln Leu Arg 1685 1695  
Thr Pro Lys Gly Lys Ser Glu Val Pro Glu Asp Leu Ala Gly Phe 1700 1710  
Ile Glu Leu Phe Gln Thr Pro Ser His Thr Lys Glu Ser Met Thr 1715 1725



Asn Glu Lys Thr Thr Lys Val Ser Tyr Arg Ala Ser Gln Pro Asp  
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Leu Val Asp Thr Pro Thr Ser Ser Lys Pro Gln Pro Lys Arg Ser  
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Leu Arg Lys Ala Asp Thr Glu Glu Phe Leu Ala Phe Arg Lys  
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Gln Thr Pro Ser Ala Gly Lys Ala Met His Thr Pro Lys Pro Ala  
1775 1780 1785

Val Gly Glu Glu Lys Asp Ile Asn Thr Phe Leu Gly Thr Pro Val  
1790 1795 1800

Gln Lys Leu Asp Gln Pro Gly Asn Leu Pro Gly Ser Asn Arg Arg  
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Leu Gln Thr Arg Lys Glu Lys Ala Gln Ala Leu Glu Glu Leu Thr  
1820 1825 1830

Gly Phe Arg Glu Leu Phe Gln Thr Pro Cys Thr Asp Asn Pro Thr  
1835 1840 1845

Ala Asp Glu Lys Thr Thr Lys Lys Ile Leu Cys Lys Ser Pro Gln  
1850 1855 1860

Ser Asp Pro Ala Asp Thr Pro Thr Asn Thr Lys Gln Arg Pro Lys  
1865 1870 1875

Arg Ser Leu Lys Lys Ala Asp Val Glu Glu Glu Phe Leu Ala Phe  
1880 1885 1890

Arg Lys Leu Thr Pro Ser Ala Gly Lys Ala Met His Thr Pro Lys  
1895 1900 1905

Ala Ala Val Gly Glu Glu Lys Asp Ile Asn Thr Phe Val Gly Thr  
1910 1915 1920

Pro Val Glu Lys Leu Asp Leu Leu Gly Asn Leu Pro Gly Ser Lys  
1925 1930 1935

Arg Arg Pro Gln Thr Pro Lys Glu Lys Ala Lys Ala Leu Glu Asp  
1940 1945 1950

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1955 1960 1965

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1970 1975 1980

Pro Gln Pro Asp Pro Val Lys Thr Pro Thr Ser Ser Lys Gln Arg  
1985 1990 1995

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2000 2005 2010

Pro Val Gly Lys Leu Thr Gln Thr Ser Gly Lys Thr Thr Gln Thr  
2015 2020 2025

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Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr Pro Asp His  
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Lys Ser Pro Pro Pro Glu Ser Met Asp Thr Pro Thr Ser Thr Arg  
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Thr Asp Pro Pro Ser Val Pro Ile Cys Asp Leu Tyr Pro Asn Gly Val 120 125  
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Phe Pro Lys Gly Gln Glu Cys Glu Tyr Pro Pro Thr Gln Asp Gly Arg 135 140  
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Arg Gln Val Arg Lys Tyr Val Met Ser Trp Ile Lys Pro Gly Met Thr 185 190  
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Val Leu Gln Tyr Asp Asp Ile Cys Lys Ile Asp Phe Gly Thr His Ile 255  
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Gln Glu Val Met Glu Ser Tyr Glu Val Glu Ile Asp Gly Lys Thr Tyr 320  
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Gln Val Lys Pro Ile Arg Asn Leu Asn Gly His Ser Ile Gly Gln Tyr 335  
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Arg Ile His Ala Gly Lys Thr Val Pro Ile Val Lys Gly Gly Glu Ala 350  
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Thr Gly Lys Gly Val Val His Asp Asp Met Glu Cys Ser His Tyr Met 380  
370 375  
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Met Ser His Leu Ala Gln His Arg Arg Ile His Thr Gly Glu Lys Pro 175  
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Ala Gln His Gln Arg Ile His Thr Gly Glu Lys Pro Tyr Lys Cys Asn 205  
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210 215  
Thr Ile His Thr Gly Glu Lys Pro Tyr Glu Cys Asn Lys Cys Gly Lys 240  
225 230 235  
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Gly Glu Lys Pro Tyr Arg Cys Asn Val Cys Gly Lys Val Phe Ser His 270  
260 265  
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Val Asn His Trp Arg Ile His Thr Gly Glu Lys Pro Tyr Lys Cys Asn 320  
305 310 315  
Glu Cys Gly Lys Val Phe Ser Arg Asn Ser Tyr Leu Ala Gln His Leu 335  
325 330  
Ile Ile His Ala Gly Glu Lys Pro Tyr Lys Cys Asp Glu Cys Asp Lys 350  
340 345  
Ala Phe Ser Gln Asn Ser His Leu Val Gln His His Arg Ile His Thr

335	360	365
Gly Glu Lys Pro Tyr Lys Cys Asp Glu Cys Gly Lys Val Phe Ser Gin		
370	375	380
Asn Ser Tyr Leu Ala Tyr His Trp Arg Ile His Thr Gly Glu Lys Ala		
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Tyr Lys Cys Asn Glu Cys Gly Lys Val Phe Gly Leu Asn Ser Ser Leu		
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Ala His His Arg Lys Ile His Thr Gly Glu Lys Pro Phe Lys Cys Asn		
420	425	430
Glu Cys Gly Lys Ala Phe Ser Met Arg Ser Ser Leu Thr Asn His His		
435	440	445
Ala Ile His Thr Gly Glu Lys His Phe Lys Cys Asn Glu Cys Gly Lys		
450	455	460
Leu Phe Arg Asp Asn Ser Tyr Leu Val Arg His Glu Arg Phe His Ala		
465	470	475
Gly Lys Lys Ser Asn Thr Cys Asn		
485		
<210> 202		
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<212> PRT		
<213> Homo sapiens		
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Met Leu Ser Val Arg Val Ala Ala Val Val Arg Ala Leu Pro Arg		
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Arg Ala Gly Leu Val Ser Arg Asn Ala Leu Gly Ser Ser Phe Ile Ala		
20	25	30
Ala Arg Asn Phe His Ala Ser Asn Thr His Leu Glu Lys Thr Gly Thr		
35	40	45
Ala Glu Met Ser Ser Ile Leu Glu Glu Arg Ile Leu Gly Ala Asp Thr		
50	55	60
Ser Val Asp Leu Glu Thr Gly Arg Val Leu Ser Ile Gly Asp Gly		
65	70	75
Ile Ala Arg Val His Gly Leu Arg Asn Val Glu Ala Glu Met Val		
85	90	95
Glu Phe Ser Ser Gly Leu Lys Gly Met Ser Leu Asn Leu Glu Pro Asp		
100	105	110
Asn Val Gly Val Val Phe Gly Asn Asp Lys Leu Ile Lys Glu Gly		
115	120	125
Asp Ile Val Lys Arg Thr Gly Ala Ile Val Asp Val Pro Val Gly Glu		
130	135	140
Glu Leu Leu Gly Arg Val Val Asp Ala Leu Gly Asn Ala Ile Asp Gly		

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145	150	155	160
Lys Gly Pro Ile Gly Ser Lys Thr Arg Arg Arg Val Gly Leu Lys Ala	165	170	175
Pro Gly Ile Ile Pro Arg Ile Ser Val Arg Glu Pro Met Glu Thr Gly	180	185	190
Ile Lys Ala Val Asp Ser Leu Val Pro Ile Gly Arg Gly Glu Arg Glu	195	200	205
Leu Ile Ile Gly Asp Arg Glu Thr Gly Lys Thr Ser Ile Ala Ile Asp	210	215	220
Thr Ile Ile Asn Glu Lys Arg Phe Asn Asp Gly Ser Asp Glu Lys Lys	225	230	235
Lys Leu Tyr Cys Ile Tyr Val Ala Ile Gly Glu Lys Arg Ser Thr Val	240	245	250
Ala Glu Leu Val Lys Arg Leu Thr Asp Ala Asp Ala Met Lys Tyr Thr	255	260	265
Ile Val Val Ser Ala Thr Ala Ser Asp Ala Ala Pro Leu Glu Tyr Leu	270	275	280
Ala Pro Tyr Ser Gly Cys Ser Met Gly Glu Tyr Phe Arg Asp Asn Gly	285	290	295
Lys His Ala Leu Ile Ile Tyr Asp Asp Leu Ser Lys Glu Ala Val Ala	300	305	310
Tyr Arg Glu Met Ser Leu Leu Arg Arg Pro Pro Gly Arg Glu Ala	315	320	325
Tyr Pro Gly Asp Val Phe Tyr Leu His Ser Arg Leu Leu Glu Arg Ala	330	335	340
Ala Lys Met Asn Asp Ala Phe Gly Gly Gly Ser Leu Thr Ala Leu Pro	345	350	355
Val Ile Glu Thr Glu Ala Gly Asp Val Ser Ala Tyr Ile Pro Thr Asn	360	365	370
Val Ile Ser Ile Thr Asp Gly Glu Ile Phe Leu Glu Thr Glu Leu Phe	375	380	385
Tyr Lys Gly Ile Arg Pro Ala Ile Asn Val Gly Leu Ser Val Ser Arg	390	395	400
Val Gly Ser Ala Ala Glu Thr Arg Ala Met Lys Glu Val Ala Gly Thr	405	410	415
Met Lys Leu Glu Leu Ala Glu Thr Tyr Arg Glu Val Ala Phe Ala Glu	420	425	430
Phe Gly Ser Leu Asp Ala Ala Thr Glu Glu Leu Leu Ser Arg Gly	435	440	445
	450	455	460

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Val Arg Leu Thr Glu Leu Leu Lys Gln Tyr Ser Pro Met Ala  
465 470 475 480

Ile Glu Glu Gln Val Ala Val Ile Tyr Ala Gly Val Arg Gly Tyr Leu  
485 490 495

Asp Lys Leu Glu Pro Ser Lys Ile Thr Lys Phe Glu Asn Ala Phe Leu  
500 505 510

Ser His Val Val Ser Gln His Gln Ala Leu Leu Gly Thr Ile Arg Ala  
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Met Gly Lys Gly Ser Phe Lys Tyr Ala Trp Val Leu Asp Lys Leu Lys  
50 55 60

Ala Glu Arg Glu Arg Gly Ile Thr Ile Asp Ile Ser Leu Trp Lys Phe  
65 70 75 80

Glu Thr Ser Lys Tyr Tyr Val Thr Ile Ile Asp Ala Pro Gly His Arg  
85 90 95

Asp Phe Ile Lys Asn Met Ile Thr Gly Thr Ser Gln Ala Asp Cys Ala  
100 105 110

Val Leu Ile Val Ala Ala Gly Val Gly Glu Phe Glu Ala Gly Ile Ser  
115 120 125

Lys Asn Gly Gln Thr Arg Glu His Ala Leu Leu Ala Tyr Thr Leu Gly  
130 135 140

Val Lys Gln Leu Ile Val Gly Val Asn Lys Met Asp Ser Thr Glu Pro  
145 150 155 160

Pro Tyr Ser Gln Lys Arg Tyr Glu Glu Ile Val Lys Glu Val Ser Thr  
165 170 175

Tyr Ile Lys Lys Ile Gly Tyr Asn Pro Asp Thr Val Ala Phe Val Pro  
180 185 190

Ile Ser Gly Trp Asn Gly Asp Asn Met Leu Val Pro Ser Ala Asn Met  
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Pro Trp Phe Lys Gly Trp Lys Val Thr Arg Lys Asp Gly Asn Ala Ser  
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Gly Thr Thr Leu Leu Glu Ala Val Asp Cys Ile Leu Pro Pro Thr Arg  
225 230 235 240

Pro Thr Asp Lys Pro Leu Arg Leu Pro Leu Gln Asp Val Tyr Lys Ile  
245 250 255

Gly Gly Ile Gly Thr Val Pro Val Gly Arg Val Glu Thr Gly Val Leu  
260 265 270

Lys Pro Gly Met Val Val Thr Phe Ala Pro Val Asn Val Thr Thr Glu  
275 280 285

Val Lys Ser Val Glu Met His His Glu Ala Leu Ser Glu Ala Leu Pro  
290 295 300

Gly Asp Asn Val Gly Phe Asn Val Lys Asn Val Ser Val Lys Asp Val  
305 310 315 320

Arg Arg Gly Asn Val Ala Gly Asp Ser Lys Asn Asp Pro Pro Met Glu  
325 330 335

Ala Ala Gly Phe Thr Ala Gln Val Ile Ile Leu Asn His Pro Gly Gln  
340 345 350

Ile Ser Ala Gly Tyr Ala Pro Val Leu Asp Cys His Thr Ala His Ile  
355 360 365

Ala Cys Lys Phe Ala Glu Leu Lys Glu Lys Ile Asp Arg Arg Ser Gly  
370 375 380

Lys Lys Leu Glu Asp Gly Pro Lys Phe Leu Lys Ser Gly Asp Ala Ala  
385 390 395 400

Ile Val Asp Met Val Pro Gly Lys Pro Met Cys Val Glu Ser Phe Ser  
405 410 415

Asp Tyr Pro Pro Leu Gly Arg Phe Ala Val Arg Asp Met Arg Gln Thr  
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Val Ala Val Gly Val Ile Lys Ala Val Asp Lys Lys Ala Ala Gly Ala  
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Gly Lys Val Thr Lys Ser Ala Gln Lys Ala Gln Lys Ala Lys  
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 35 40 45  
 Gly Asn Val Ala Ser Asp Leu Gly Ile Val Thr Gly Ser Gly Glu Val  
 50 55 60  
 Thr Phe Ser Leu Glu Ser Gly Ser Glu Tyr Leu Lys Ile Asp Asn Leu  
 65 70 75  
 Thr Gly Glu Ser Thr Ser Glu Arg Arg Ile Asp Arg Glu Lys Leu  
 85 90 95  
 Pro Gln Cys Gln Met Ile Phe Asp Glu Asn Glu Cys Phe Leu Asp Phe  
 100 105 110  
 Glu Val Ser Val Ile Gly Pro Ser Gln Ser Trp Val Asp Leu Phe Glu  
 115 120 125  
 Gly Gln Val Ile Val Leu Asp Ile Asn Asp Asn Thr Pro Thr Phe Pro  
 130 135 140  
 Ser Pro Val Leu Thr Leu Thr Val Glu Asn Arg pro Val Gly Thr  
 145 150 155  
 Leu Tyr Leu Leu Pro Thr Ala Thr Asp Arg Asp Phe Gly Arg Asn Gly  
 165 170 175  
 Ile Glu Arg Tyr Glu Leu Leu Gln Glu pro Gly Gly Gly Ser Gly  
 180 185 190  
 Gly Glu Ser Arg Arg Ala Gly Ala Ala Asp Ser Ala Pro Tyr Pro Gly  
 195 200 205  
 Gly Gly Glu Asn Gly Ala Ser Gly Gly Gly Ser Gly Cys Ser Lys Arg  
 210 215 220  
 Arg Leu Asp Ala Ser Glu Gly Gly Gly Thr Asn Pro Gly Gly Arg  
 225 230 235  
 Ser Ser Val Phe Glu Leu Gln Val Ala Asp Thr Pro Asp Gly Glu Lys  
 245 250 255  
 Gln Pro Gln Leu Ile Val Lys Gly Ala Leu Asp Arg Glu Gln Arg Asp  
 260 265 270  
 Ser Tyr Glu Leu Thr Leu Arg Val Arg Asp Gly Gly Asp Pro Pro Arg  
 275 280 285  
 Ser Ser Gln Ala Ile Leu Arg Val Leu Ile Thr Asp Val Asn Asp Asn  
 290 295 300  
 Ser Pro Arg Phe Glu Lys Ser Val Tyr Glu Ala Asp Leu Ala Glu Asn  
 305 310 315  
 Ser Ala Pro Gly Thr Pro Ile Leu Gln Leu Arg Ala Ala Asp Leu Ser  
 320 325 330 335

Val Gly Val Asn Gly Gln Ile Glu Tyr Val Phe Gly Ala Ala Thr Glu  
 340 345 350  
 Ser Val Arg Arg Leu Leu Arg Leu Asp Glu Thr Ser Gly Trp Leu Ser  
 355 360 365  
 Val Leu His Arg Ile Asp Arg Glu Glu Val Asn Gln Leu Arg Phe Thr  
 370 375 380  
 Val Met Ala Arg Asp Arg Gly Gln Pro Pro Lys Thr Asp Lys Ala Thr  
 385 390 395 400  
 Val Val Leu Asn Ile Lys Asp Glu Asn Asp Asn Val Pro Ser Ile Glu  
 405 410 415  
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 450 455 460  
 Asp Val Pro Phe Gln Leu Lys Pro Ala Ser Asp Thr Glu Gly Asp Gln  
 465 470 475 480  
 Asn Lys Lys Lys Tyr Phe Leu His Thr Ser Thr Pro Leu Asp Tyr Glu  
 485 490 495  
 Ala Thr Arg Glu Phe Asn Val Val Ile Val Ala Val Asp Ser Gly Ser  
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 Pro Glu Asn Asn Ile Pro Gly Glu Arg Val Ala Thr Val Leu Ala Thr  
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 Asp Ala Asp Ser Gly Lys Asn Ala Glu Ile Ala Tyr Ser Leu Asp Ser  
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 Ser Val Met Gly Ile Phe Ala Ile Asp Pro Asp Ser Gly Asp Ile Leu  
 580 585 590  
 Val Asn Thr Val Leu Asp Arg Glu Gln Thr Asp Arg Tyr Glu Phe Lys  
 595 600 605  
 Val Asn Ala Lys Asp Lys Gly Ile Pro Val Leu Gln Gly Ser Thr Thr  
 610 615 620  
 Val Ile Val Gln Val Ala Asp Lys Asn Asp Asn Asp Pro Lys Phe Met  
 625 630 635 640  
 Gln Asp Val Phe Thr Phe Tyr Val Lys Glu Asn Leu Gln Pro Asn Ser  
 645 650 655

Pro Val Gly Met Val Thr Val Met Asp Ala Asp Lys Gly Arg Asn Ala 660 665 670	965 970 975	Met Gly Arg Tyr Arg Ser Val Asn Gly Gly Pro Gly Ser Pro Asp Leu 980 985 990
Glu Met Ser Leu Tyr Ile Glu Glu Asn Asn Ile Phe Ser Ile Glu 675 680 685		Ala Arg His Tyr Lys Ser Ser Ser Pro Leu Pro Thr Val Gln Leu His 995 1000 1005
Asn Asp Thr Gly Thr Ile Tyr Ser Thr Met Ser Phe Asp Arg Glu His 690 695 700		Pro Gln Ser Pro Thr Ala Gly Lys Lys His Gln Ala Val Gln Asp 1010 1015 1020
Gln Thr Thr Tyr Phe Arg Val Lys Ala Val Asp Gly Gly Asp Pro 705 710 715		Leu Pro Pro Ala Asn Thr Phe Val Gly Ala Gly Asp Asn Ile Ser 1025 1030 1035
Pro Arg Ser Ala Thr Ala Thr Val Ser Leu Phe Val Met Asp Glu Asn 720 725 730		Ile Gly Ser Asp His Cys Ser Glu Tyr Ser Cys Gln Thr Asn Asn 1040 1045 1050
Asp Asn Ala Pro Thr Val Thr Leu Pro Lys Asn Ile Ser Tyr Thr Leu 740 745 750		Lys Tyr Ser Lys Gln Met Arg Leu His Pro Tyr Ile Thr Val Phe 1055 1060 1065
Leu Pro Pro Ser Ser Asn Val Arg Thr Val Val Ala Thr Val Leu Ala 755 760 765	Gly	
Thr Asp Ser Asp Asp Gly Ile Asn Ala Asp Leu Asn Tyr Ser Ile Val 770 775 780	<210> 205	
Gly Gly Asn Pro Phe Lys Leu Phe Glu Ile Asp Pro Thr Ser Gly Val 785 790 795	<211> 401	
Val Ser Leu Val Gly Lys Leu Thr Gln Lys His Tyr Gly Leu His Arg 800 805 810	<212> PRT	
Leu Val Val Gln Val Asn Asp Ser Gly Gln Pro Ser Gln Ser Thr Thr 820 825 830	<213> Homo sapiens	
Thr Val Val His Val Phe Val Asn Glu Ser Val Ser Asn Ala Thr Ala 835 840 845	<400> 205	
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Ile Ala Gly Asp Pro Ser Tyr Glu Ile Ser Lys Gln Arg Leu Ser Ile 865 870 875	Asn Pro Ile Leu Ala Ser Leu Gln His Asn Ser Ile Leu Thr Pro Thr 20 25 30	
Val Ile Gly Val Val Ala Gly Ile Met Thr Val Ile Leu Ile Ile Leu 880 885 890	Arg Val Ser Ser Ala Thr Lys Gln Lys Val Leu Ser Pro Pro His 35 40 45	
Ile Val Val Met Ala Arg Tyr Cys Arg Ser Lys Asn Lys Asn Gly Tyr 900 905 910	Ile Lys Ala Asp Phe Asn Leu Ala Asp Phe Glu Cys Glu Glu Asp Pro 50 55 60	
Glu Ala Gly Lys Lys Asp His Glu Asp Phe Thr Pro Gln Gln His 915 920 925	Phe Asp Asn Leu Glu Leu Lys Thr Ile Asp Glu Lys Glu Glu Leu Arg 65 70 75	
Asp Lys Ser Lys Lys Pro Lys Lys Asp Lys Lys Asn Lys Ser Lys 930 935 940	Asn Ile Leu Val Gly Thr Thr Gly Pro Ile Met Ala Gln Leu Leu Asp 85 90 95	
Gln Pro Leu Tyr Ser Ser Ile Val Thr Val Glu Ala Ser Lys Pro Asn 945 950 955	Asn Asn Leu Pro Arg Gly Gly Ser Gly Ser Val Leu Gln Asp Glu Glu 100 105 110	
Gly Gln Arg Tyr Asp Ser Val Asn Glu Lys Leu Ser Asp Ser Pro Ser 960 965 968	Val Leu Ala Ser Leu Glu Arg Ala Thr Leu Asp Phe Lys Pro Leu His 115 120 125	
	Lys Pro Asn Gly Phe Ile Thr Leu Pro Gln Leu Gly Asn Cys Glu Lys 130 135 140	
	Met Ser Leu Ser Lys Val Ser Leu Pro Ile Pro Ala Val Ser 145 150 155	
	Asn Ile Lys Ser Leu Ser Phe Pro Lys Leu Asp Ser Asp Asp Ser Asn 160 165 168	



165 170 175

Gln Lys Thr Ala Lys Leu Ala Ser Thr Phe His Ser Thr Ser Cys Leu  
180 185 190

Arg Asn Gly Thr Phe Gln Asn Ser Leu Lys Pro Ser Thr Gln Ser Ser  
195 200 205

Ala Ser Gly Leu Asn Gly His His Thr Leu Gly Leu Ser Ala Leu Asn  
210 215 220

Leu Asp Ser Gly Thr Glu Met Pro Ala Leu Thr Ser Ser Gln Met Pro  
225 230 235

Ser Leu Ser Val Leu Ser Val Cys Thr Glu Glu Ser Ser Pro Pro Asn  
240 245 250 255

Thr Gly Pro Thr Val Thr Pro Pro Asn Phe Ser Val Ser Gln Val Pro  
260 265 270

Asn Met Pro Ser Cys Pro Gln Ala Tyr Ser Glu Leu Gln Met Leu Ser  
275 280 285

Pro Ser Glu Arg Gln Cys Val Glu Thr Val Val Asn Met Gly Tyr Ser  
290 295 300

Tyr Glu Cys Val Leu Arg Ala Met Lys Lys Gly Glu Asn Ile Glu  
305 310 315 320

Gln Ile Leu Asp Tyr Leu Phe Ala His Gly Gln Leu Cys Glu Lys Gly  
325 330 335

Phe Asp Pro Leu Leu Val Glu Glu Ala Leu Glu Met His Gln Cys Ser  
340 345 350

Glu Glu Lys Met Met Glu Phe Leu Gln Leu Met Ser Lys Phe Lys Glu  
355 360 365

Met Gly Phe Glu Leu Lys Asp Ile Lys Glu Val Leu Leu Leu His Asn  
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Asn Asp Gln Asp Asn Ala Leu Glu Asp Leu Met Ala Arg Ala Gly Ala  
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Ser

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Cys Leu Phe Pro Arg Val Phe Ala Ala Glu Ala Val Thr Ala Asp Ser  
20 25 30

Glu Val Leu Glu Glu Arg Gln Lys Arg Leu Pro Tyr Val Pro Glu Pro

35 40 45

Tyr Tyr Pro Glu Ser Gly Trp Asp Arg Leu Arg Glu Leu Phe Gly Lys  
50 55 60

Asp Glu Gln Gln Arg Ile Ser Lys Asp Leu Ala Asn Ile Cys Lys Thr  
65 70 75 80

Ala Ala Thr Ala Gly Ile Ile Gly Trp Val Tyr Gly Gly Ile Pro Ala  
85 90 95

Phe Ile His Ala Lys Gln Gln Tyr Ile Glu Gln Ser Gln Ala Glu Ile  
100 105 110

Tyr His Asn Arg Phe Asp Ala Val Gln Ser Ala His Arg Ala Ala Thr  
115 120 125

Arg Gly Phe Ile Arg Tyr Gly Trp Arg Trp Gly Trp Arg Thr Ala Val  
130 135 140

Phe Val Thr Ile Phe Asn Thr Val Asn Thr Ser Leu Asn Val Tyr Arg  
145 150 155 160

Asn Lys Asp Ala Leu Ser His Phe Val Ile Ala Gly Ala Val Thr Gly  
165 170 175

Ser Leu Phe Arg Ile Asn Val Gly Leu Arg Gly Leu Val Ala Gly Gly  
180 185 190

Ile Ile Gly Ala Leu Leu Gly Thr Pro Val Gly Gly Leu Leu Met Ala  
195 200 205

Phe Gln Lys Tyr Ser Gly Glu Thr Val Gln Glu Arg Lys Gln Lys Asp  
210 215 220

Arg Lys Ala Leu His Glu Leu Lys Leu Glu Trp Lys Gly Arg Leu  
225 230 235 240

Gln Val Thr Glu His Leu Leu Pro Glu Lys Ile Glu Ser Ser Leu Gln Glu  
245 250 255

Asp Glu Pro Glu Asn Asp Ala Lys Lys Ile Glu Ala Leu Leu Asn Leu  
260 265 270

Pro Arg Asn Pro Ser Val Ile Asp Lys Gln Asp Lys Asp  
275 280 285

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Met Leu Asn Lys Val Leu Ser Arg Leu Gly Val Ala Gly Gln Trp Arg  
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Phe Val Asp Val Leu Gly Leu Glu Glu Ser Leu Gly Ser Val Pro  
20 25 30

Ala Pro Ala Cys Ala Leu Leu Leu Phe Pro Leu Thr Ala Gln His

35 40 45

Glu An Phe Arg Lys Lys Gln Ile Glu Glu Leu Lys Gly Gln Glu Val  
50 55 60

Ser Pro Lys Val Tyr Phe Met Lys Gln Thr Ile Gly Asn Ser Cys Gly  
65 70 75 80

Thr Ile Gly Leu Ile His Ala Val Ala Asn Asn Gln Asp Lys Leu Gly  
85 90 95

Phe Glu Asp Gly Ser Val Leu Lys Gln Phe Leu Ser Glu Thr Glu Lys  
100 105 110

Met Ser Pro Glu Asp Arg Ala Lys Cys Phe Glu Lys Asn Glu Ala Ile  
115 120 125

Gln Ala His Asp Ala Val Ala Gln Glu Gly Gln Cys Arg Val Asp  
130 135 140

Asp Lys Val Asn Phe His Phe Ile Leu Phe Asn Asn Val Asp Gly His  
145 150 155 160

Leu Tyr Glu Leu Asp Gly Arg Met Pro Phe Leu Val Asn His Gly Ala  
165 170 175

Ser Ser Glu Asp Thr Leu Leu Lys Asp Ala Ala Lys Val Cys Arg Glu  
180 185 190

Phe Thr Glu Arg Glu Gln Gly Glu Val Arg Phe Ser Ala Val Ala Leu  
195 200 205

Cys Lys Ala Ala  
210

<210> 208  
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Met Ser Leu Ser Met Arg Asp Pro Val Ile Pro Gly Thr Ser Met Ala  
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Tyr His Pro Phe Leu Pro His Arg Ala Pro Asp Phe Ala Met Ser Ala  
20 25 30

Val Leu Gly His Gln Pro Pro Phe Phe Pro Ala Leu Thr Leu Pro Pro  
35 40 45

Asn Gly Ala Ala Leu Ser Leu Pro Gly Ala Leu Ala Lys Pro Ile  
50 55 60

Met Asp Gln Leu Val Gly Ala Ala Glu Thr Gly Ile Pro Phe Ser Ser  
65 70 75 80

Leu Gly Pro Gln Ala His Leu Arg Pro Leu Lys Thr Met Glu Pro Glu  
85 90 95

Glu Glu Val Glu Asp Asp Pro Lys Val His Leu Glu Ala Lys Glu Leu

100 105 110

Trp Asp Gln Phe His Lys Arg Gly Thr Glu Met Val Ile Thr Lys Ser  
115 120 125

Gly Arg Arg Met Phe Pro Pro Phe Lys Val Arg Cys Ser Gly Leu Asp  
130 135 140

Lys Lys Ala Lys Tyr Ile Leu Leu Met Asp Ile Ile Ala Ala Asp Asp  
145 150 155 160

Cys Arg Tyr Lys Phe His Asn Ser Arg Trp Met Val Ala Gly Lys Ala  
165 170 175

Asp Pro Glu Met Pro Lys Arg Met Tyr Ile His Pro Asp Ser Pro Ala  
180 185 190

Thr Gly Glu Gln Trp Met Ser Lys Val Val Thr Phe His Lys Leu Lys  
195 200 205

Leu Thr Asn Asn Ile Ser Asp Lys His Gly Phe Thr Leu Ala Phe Pro  
210 215 220

Ser Asp His Ala Thr Trp Gln Gly Asn Tyr Ser Phe Gly Thr Gln Thr  
225 230 235 240

Ile Leu Asn Ser Met His Lys Tyr Gln Pro Arg Phe His Ile Val Arg  
245 250 255

Ala Asn Asp Ile Leu Lys Leu Pro Tyr Ser Thr Phe Arg Thr Tyr Leu  
260 265 270

Phe Pro Glu Thr Glu Phe Ile Ala Val Thr Ala Tyr Gln Asn Asp Lys  
275 280 285

Ile Thr Gln Leu Lys Ile Asp Asn Asn Pro Phe Ala Lys Gly Phe Arg  
290 295 300

Asp Thr Gly Asn Gly Arg Arg Glu Lys Arg Gln Gln Leu Thr Leu Gln  
305 310 315 320

Ser Met Arg Val Phe Asp Glu Arg His Lys Lys Glu Asn Gly Thr Ser  
325 330 335

Asp Glu Ser Ser Ser Glu Gln Ala Phe Asn Cys Phe Ala Gln Ala  
340 345 350

Ser Ser Pro Ala Ala Ser Thr Val Gly Thr Ser Asn Leu Lys Asp Leu  
355 360 365

Cys Pro Ser Glu Gly Glu Ser Asp Ala Glu Ala Glu Ser Lys Glu Glu  
370 375 380

His Gly Pro Glu Ala Cys Asp Ala Ala Lys Ile Ser Thr Thr Thr Ser  
385 390 395 400

Glu Glu Pro Cys Arg Asp Lys Gly Ser Pro Ala Val Lys Ala His Leu  
405 410 415

Phe Ala Ala Glu Arg Pro Arg Asp Ser Gly Arg Leu Asp Lys Ala Ser  
420 425 430

Pro Asp Ser Arg His Ser Pro Ala Thr Ile Ser Ser Ser Thr Arg Gly  
435 440 445

Leu Gly Ala Glu Glu Arg Arg Ser Pro Val Arg Glu Gly Thr Ala Pro  
450 455 460

Ala Lys Val Glu Glu Ala Arg Ala Leu Pro Gly Lys Glu Ala Phe Ala  
465 470 475 480

Pro Leu Thr Val Gln Thr Asp Ala Ala Arg Ser Ser Val His Arg His  
485 490 495

Pro Phe Arg Asn Leu Asn Thr Met Arg Pro Arg Leu Arg Tyr Ser Pro  
500 505 510

Tyr Ser Ile Pro Val Pro Val Pro Asp Gly Ser Ser Leu Leu Thr Thr  
515 520 525

Ala Leu Ala Ala Ser Pro Ala Ser Val Ala Val Asp Ser Gly Ser Glu  
530 535 540

Leu Asn Ser Arg Ser Ser Thr Leu Ser Ser Ser Ser Met Ser Leu Ser  
545 550 555 560

Pro Lys Leu Cys Ala Glu Lys Glu Ala Ala Thr Ser Glu Leu Gln Ser  
565 570 575

Ile Gln Arg Leu Val Ser Gly Leu Glu Ala Lys Pro Asp Arg Ser Arg  
580 585 590

Ser Ala Ser Pro  
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Asp Ala Ser Val Asn Phe Ser Glu Phe Ser Lys Lys Cys Ser Glu Arg  
35 40 45

Trp Lys Thr Met Ser Ala Lys Glu Lys Gly Lys Phe Glu Asp Met Ala  
50 55 60

Lys Ala Asp Lys Ala Arg Tyr Glu Arg Glu Met Lys Thr Tyr Ile Pro  
65 70 75 80

Pro Lys Gly Glu Thr Lys Lys Lys Phe Lys Asp Pro Asn Ala Pro Lys  
85 90 95

Arg Pro Pro Ser Ala Phe Phe Leu Phe Cys Ser Glu Tyr Tyr Arg Pro Lys  
100 105 110

Ile Lys Gly Glu His Pro Gly Leu Ser Ile Gly Asp Val Ala Lys Lys  
115 120 125

Leu Gly Glu Met Trp Asn Asn Thr Ala Ala Asp Asp Lys Gln Pro Tyr  
130 135 140

Glu Lys Lys Ala Ala Lys Leu Lys Glu Lys Tyr Glu Lys Asp Ile Ala  
145 150 155 160

Ala Tyr Arg Ala Lys Gly Lys Pro Asp Ala Ala Lys Lys Gly Val Val  
165 170 175

Lys Ala Glu Lys Ser Lys Lys Lys Glu Glu Glu Glu Asp Glu Glu  
180 185 190

Asp Glu Glu Asp Glu Glu Glu Glu Asp Glu Glu Asp Glu Asp Glu  
195 200 205

Glu Glu Asp Asp Asp Glu  
210 215

<210> 210  
<211> 243  
<212> PRT  
<213> Homo sapiens  
<400> 210

Met Ala Ala Ile Ala Ala Ser Glu Val Leu Val Asp Ser Ala Glu Glu  
1 5 10 15

Gly Ser Leu Ala Ala Ala Glu Leu Ala Ala Gln Lys Arg Glu Gln  
20 25 30

Arg Leu Arg Lys Phe Arg Glu Leu His Leu Met Arg Asn Glu Ala Arg  
35 40 45

Lys Leu Asn His Gln Glu Val Val Glu Glu Asp Lys Arg Leu Lys Leu  
50 55 60

Pro Ala Asn Trp Glu Ala Lys Lys Lys Ala Arg Leu Glu Trp Glu Leu Lys  
65 70 75 80

Glu Glu Glu Lys Lys Lys Glu Cys Ala Ala Arg Gly Glu Asp Tyr Glu  
85 90 95

Lys Val Lys Leu Leu Glu Ile Ser Ala Glu Asp Ala Glu Arg Trp Glu  
100 105 110

Arg Lys Lys Lys Arg Lys Asn Pro Asp Leu Gly Phe Ser Asp Tyr Ala  
115 120 125

Ala Ala Gln Leu Arg Gln Tyr His Arg Leu Thr Lys Gln Ile Lys Pro  
130 135 140

Asp Met Glu Thr Tyr Glu Arg Leu Arg Glu Lys His Gly Glu Glu Phe  
145 150 155 160

Phe Pro Thr Ser Asn Ser Leu Leu His Gly Thr His Val Pro Ser Thr  
165 170 175  
Glu Glu Ile Asp Arg Met Val Ile Asp Leu Glu Lys Gln Ile Glu Lys  
180 185 190  
Arg Asp Lys Tyr Ser Arg Arg Asp Pro Tyr Asn Asp Ala Asp Ile  
195 200 205  
Asp Tyr Ile Asn Glu Arg Asn Ala Lys Phe Asn Lys Lys Ala Glu Arg  
210 215 220  
Phe Tyr Gly Lys Tyr Thr Ala Glu Ile Lys Gln Asn Leu Glu Arg Gly  
225 230 235  
Thr Ala Val  
240  
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<213> Homo sapiens  
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Gln Thr Trp Glu Ser Glu Gly Ser Ile Lys Lys Ala Gln Gln Ala  
20 25 30  
Val Ala Asn Lys Ala Leu Thr Glu Ser Thr Leu Pro Lys Pro Val Gln  
35 40 45  
Lys Pro Pro Lys Ser Asn Val Asn Asn Asn Pro Gly Ser Ile Thr Pro  
50 55 60  
Thr Val Glu Leu Asn Gly Leu Ala Met Lys Arg Gly Glu Pro Ala Ile  
65 70 75  
Tyr Arg Pro Leu Asp Pro Lys Pro Phe Pro Asn Tyr Arg Ala Asn Tyr  
85 90 95  
Asn Phe Arg Gly Met Tyr Asn Gln Arg Tyr His Cys Pro Val Pro Lys  
100 105 110  
Ile Phe Tyr Val Gln Leu Thr Val Gly Asn Asn Glu Phe Phe Gly Glu  
115 120 125  
Gly Lys Thr Arg Gln Ala Ala Arg His Asn Ala Ala Met Lys Ala Leu  
130 135 140  
Gln Ala Leu Gln Asn Glu Pro Ile Pro Glu Arg Ser Pro Gln Asn Gly  
145 150 155  
Glu Ser Gly Lys Asp Met Asp Asp Lys Asp Ala Asn Lys Ser Glu  
165 170 175  
Ile Ser Leu Val Phe Glu Ile Ala Leu Lys Arg Asn Met Pro Val Ser  
180 185 190

Phe Glu Val Ile Lys Glu Ser Gly Pro Pro His Met Lys Ser Phe Val  
195 200 205  
Thr Arg Val Ser Val Gly Glu Phe Ser Ala Glu Gly Glu Gly Asn Ser  
210 215 220  
Lys Lys Leu Ser Lys Lys Arg Ala Ala Thr Thr Val Leu Gln Glu Leu  
225 230 235  
Lys Lys Leu Pro Pro Leu Pro Val Val Glu Lys Pro Lys Leu Phe Phe  
245 250 255  
Lys Lys Arg Pro Lys Thr Ile Val Lys Ala Gly Pro Glu Tyr Gly Gln  
260 265 270  
Gly Met Asn Pro Ile Ser Arg Leu Ala Gln Ile Gln Gln Ala Lys Lys  
275 280 285  
Glu Lys Glu Pro Asp Tyr Val Leu Leu Ser Glu Arg Gly Met Pro Arg  
290 295 300  
Arg Arg Glu Phe Val Met Gln Val Lys Val Gly Asn Glu Val Ala Thr  
305 310 315  
Gly Thr Gly Pro Asn Lys Lys Ile Ala Lys Lys Asn Ala Ala Glu Ala  
325 330 335  
Met Leu Leu Gln Leu Gly Tyr Lys Ala Ser Thr Asn Leu Gln Asp Gln  
340 345 350  
Leu Glu Lys Thr Gly Glu Asn Lys Lys Gly Trp Ser Gly Pro Lys Pro Gly  
355 360 365  
Phe Pro Glu Pro Thr Asn Asn Thr Pro Lys Gly Ile Leu His Leu Ser  
370 375 380  
Pro Asp Val Tyr Gln Glu Met Glu Ala Ser Arg His Lys Val Ile Ser  
385 390 395  
Gly Thr Thr Leu Gly Tyr Leu Ser Pro Lys Asp Met Asn Gln Pro Ser  
405 410 415  
Ser Ser Phe Phe Ser Ile Ser Pro Thr Ser Asn Ser Ser Ala Thr Ile  
420 425 430  
Ala Arg Glu Leu Leu Met Asn Gly Thr Ser Ser Thr Ala Glu Ala Ile  
435 440 445  
Gly Leu Lys Gly Ser Ser Pro Thr Pro Pro Cys Ser Pro Val Gln Pro  
450 455 460  
Ser Lys Gln Leu Glu Tyr Leu Ala Arg Ile Gln Gly Phe Gln Val  
465 470 475

# ABE, IKUBO & KATAYAMA

FUKUOKA BUILDING 2-8-7, YAESU, CHUO-KU,  
TOKYO 104-0028, JAPAN  
TEL 81-3-3273-2600 FAX 81-3-3273-2033  
(Patent Division Direct)  
TEL 81-3-3273-2611 FAX 81-3-3273-2034

MORIO TAKESHITA  
(Of Counsel)  
SHOGO ABE  
YASUHIKO IKUBO  
EIJI KATAYAMA  
HISASHI ITO  
ISAO SAIKI  
JUNICHI KITAHARA  
KAZUYUKI TAGUCHI  
MASARU UETAKE  
KOJI HAYASHI  
MASAHIRO OTSUKI  
HIDETO SASAKI  
SUMIKO KOBAYASHI  
  
MAMI HINO

HIROKAZU HONDA  
MAKOTO HATTORI  
SHINO HIROSE  
TAKAFUMI HARADA  
NAHO EBATA  
TSUYOSHI DAI  
AYA FUJIMATSU  
HIROFUMI KATO  
AKIKO KOJIMA  
TOSHIYASU SUZAKI  
GAKU IIDA  
CHIZUKO NAKANDAKARI  
GO ARAI  
SEIICHI AMINO  
KOJI TAKITANI  
NAOMI TSUDA

(Patent Division)  
TAKASHI AOKI  
(Of Counsel)  
HIROSHI KOBAYASHI  
  
KAORU KURODA  
TAKAYUKI HIROSE  
NOBUSHIGE FURUHASHI  
NORIO OHMORI  
RYOKO OSHIKAMO  
KYOKO TAMURA  
YASUHITO SUZUKI  
TAKASHI FUJITA

December 17, 2004

Edwards & Angell, LLP  
101 Federal Street Boston,  
MA02110-1800  
U.S.A.  
Fax: +1-617-439-4170

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Our Ref.: P03-0038US

**Please file this application Before December 26, 2004**

Re : New National Phase Application in U.S.A. derived from PCT/JP2003/008036  
in the name of TAKEDA PHARMACEUTICAL COMPANY LIMITED

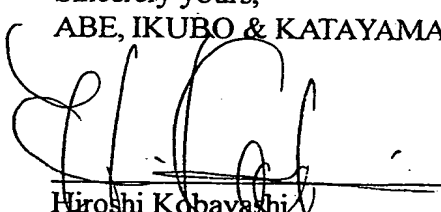
Dear Sirs:

Please proceed with the national entry from the above-identified PCT international application before a 30-month deadline of December 26, 2004.

Please refer to the Additional Instructions and Filing Particulars Sheet. If anything further is required for the national entry, please so inform us immediately.

We thank you for your cooperation with this new case and kindly ask you to acknowledge safe receipt of this letter by return facsimile.

Sincerely yours,  
ABE, IKUBO & KATAYAMA

  
Hiroshi Kobayashi  
Patent Attorney

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Filing Particular Sheet

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End of Text.

Regarding the references  
for IDS, we send you  
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## Filing Particulars

Takeda's Case No. 3060US0P,EP0W

Our Ref: P03-0038US,EP

(1) Title of the Invention

Preventing/Treating Agent for Cancer

(2) Applicant

Name: TAKEDA PHARMACEUTICAL COMPANY LIMITED

Address: 1-1, Doshomachi 4-chome, Chuo-ku, Osaka-shi, Osaka 541-0045 JAPAN

(3) Inventors

(A) Name: Hiroshi TANAKA

Address: 6-3-404, Ninomiya 4-chome, Tsukuba-shi, Ibaraki 305-0051 JAPAN

(B) Name: Isao KAIEDA

Address: 22-1-302, Kasuga 2-chome, Tsukuba-shi, Ibaraki 305-0821 JAPAN

(C) Name: Kohei HONDA

Address: 15-19-302, Kasuga 3-chome, Tsukuba-shi, Ibaraki 305-0821 JAPAN

(4) Pct International Application

Application No. PCT/JP2003/008036

Filing Date: June 25, 2003

(5) Japanese Patent Application(s) from which the present application claims priority

Country	Date of Filing	Application No.	Priority
a) Japan	June 26, 2002	186799/2002	yes
b) Japan	June 26, 2002	186815/2002	yes

a) Applicant: The same as above (2)

Inventors: (A) , (B) and (C)

b) Applicant: The same as above (2)

Inventors: (A) and (B)